

ELLIS HORWOOD SERIES IN ANALYTICAL CHEMISTRY

# EDUCATION AND TEACHING IN ANALYTICAL CHEMISTRY

G. E. Baiulescu C. Patroescu R. A. Chalmers

The Ellis Horwood series in  
**ANALYTICAL CHEMISTRY**  
Series Editors: Dr. R. A. CHALMERS and Dr. M.  
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of Aberdeen

## **EDUCATION AND TEACHING IN ANALYTICAL CHEMISTRY**

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This book strongly supports the contention that modern analytical chemistry is, as well as being multi-disciplinary, a unified and independent scientific discipline which participates with other sciences in the optimization and development of many processes in modern technology. In the development and training of an analyst, to equip him to tackle the current problems of chemical analysis, the teaching and education he receives play an important role.

This work lays out all the educational requirements in analytical chemistry. It promotes the concept of the analytical chemistry student being 'situation-oriented', deliberately encouraged to educate himself. It takes the view that teaching in analytical chemistry plays the role of the catalyst in promoting the process of learning; that teaching is a constituent part of a general education process, carried out in a serious scholarly atmosphere, where the student is taught to think independently and draw from his own ability the capacity to understand, and successfully apply, the accumulated experience of his scientific knowledge.

The authors stress their conviction that such education is achieved primarily through the medium of the lecture course, where the necessity lies in logical, sequential presentation of the fundamentals both by the lecturer and by specialist texts; clear, concise wording to the material; the value of audio-visual aids, e.g. blackboard, slides, television; and the succinct delivery of the lecture with effective use of the voice. It also advises on the supplementation of the lecture course with suitable reading material, which should be read in relation to the experiments of practical courses.

**Readership:** Teachers and lecturers in analytical chemistry, and all its related disciplines, in universities, polytechnics, technical colleges, and other educational establishments, e.g. adult education centres; and teacher training establishments.

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# Preface

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This book arose from the authors' conviction that the days are long gone when analytical chemistry could be regarded as only the servant of other branches of chemistry. This notion that analytical chemistry is in some way inferior as an academic discipline originated with Ostwald, who conveniently forgot that without analysis our understanding of chemistry could never have come into existence. The ever increasing demands made on the analyst by advances in technology and science mean that, more than ever before, the analyst must be equipped with a wide and sound knowledge not only of chemistry, but of physics, electronics, statistics, biology and so on. It is therefore most important that this should be recognized by chemists in general, and proper provision made in undergraduate curricula for analytical chemistry to be taught by specialists in the subject, who can show its proper relationship to the other branches of chemistry, and also impart to the students the special nature of the analytical approach, which is in essence that of problem solving. Every analysis, however routine it may appear, can pose problems, since the unforeseen may happen, and unless the analyst is always on his guard he may be caught unawares and produce an erroneous result. In many instances, new kinds of sample, unexpected combinations of elements, inhomogeneity, and many other sources of difficulty, will compel the analyst to think, and think hard, before deciding on the best approach to take. Edison said 'There is no expedient to which the human mind will not turn, to avoid the sheer hard labour of thinking'. There is no escape from the fact that analytical chemistry requires continuous thought, as well as considerable manual skill and dexterity, and very often an almost encyclopaedic knowledge of chemistry and its literature. The analyst needs a very wide range of skills and training, and this book is intended to set out some thoughts on how the necessary learning may be imparted to him. It is not intended as a guide to courses of instruction — each teacher should have his own ideas on how to teach, and what to teach — but is certainly meant to encourage the reader to *think*.

The authors are most grateful to various copyright holders for their kind permission to use copyright material, and also to Professors Laitinen, Enke and Irving. Acknowledgement is made at appropriate points in the text, and is also due to Random House Inc., for permission to use the excerpt from *Faust*, to MIT Press for use of the excerpts from *God and Golem Inc.*

The Authors

To Lucia, Maria and Grace,  
who put up with so much

# Introduction

Analytical chemistry, like Cleopatra's beauty, is of infinite variety [1]

---

The aim of this book is to expose the basic idea that analytical chemistry is an independent science, as well as to emphasize the role of teaching and of education in analytical chemistry and chemical analysis.

To write a book on science is a difficult task, irrespective of its field. It is even more difficult to write a book about the educational processes necessary for assimilation of knowledge in a given area of science, since it involves a general survey, both logical and critical, of that area and, of course, interconnections with other sciences.

The 'information explosion' characteristic of recent years makes a complete knowledge of the literature almost impossible. Hence the book will be essentially based on fundamental articles, books and reviews and to a smaller extent on specialized scientific papers having a bearing on the topic.

According to Kolthoff [2] "Analytical chemistry, like the other fields of chemistry is in a state of flux. With all of the modern developments particularly in physical methods of analysis, emphasis in analytical chemistry has changed today to a great extent from wet analytical chemistry to instrumental analytical techniques. ... At the moment the analytical chemist is becoming more and more part of a team, who together with his colleagues in other fields of chemistry are going to answer the problems which not only occur in industry and 'pure' research but also in our environment". This supports our contention that modern analytical chemistry, despite its apparent multidisciplinary character, is a unified and independent scientific discipline which participates with other sciences in the optimization and development of many processes in modern technology as well as standing alongside the other branches of chemistry in the general development of that science.

According to Siggia [3] "The most important characteristics of a primary analytical man are: self-confidence, drive, love of subject, aggressiveness, tenacity, technical ability, and the ability to work with others". An analyst who fulfils these requirements is equipped to tackle the main current problems of chemical

analysis, such as on-line analysis, environmental analysis, clinical analysis, oceanography, etc. The principal qualification of the 'primary analytical man' is that he be 'situation oriented'.

In the development of such workers, teaching and education in analytical chemistry play a preponderant role.

Laidler [4] wrote: "I deliberately said 'help our students to educate themselves' rather than 'help to educate our students', because I am convinced that the educator cannot hope to be more than a catalyst in the educational process".

In other words, teaching in analytical chemistry plays the role of a catalyst in promoting the process itself, namely education in analytical chemistry.

As Anatole France wrote, "Do not try to satisfy your vanity by teaching a great many things. Awaken your students' curiosity. It is enough to open their minds, without overloading them. Put into them just a spark; if there is some inflammable stuff it will catch fire".

It follows that teaching must be a constituent part of a general educational process which must not be confused with education itself. Teaching is efficient only if it is carried out in a serious scholarly atmosphere, in which the student will really want to educate himself. The etymological dictionaries indicate that the word education should signify drawing out; that is, in the present context, leading the student to think independently and to draw out of his own ability the capacity to understand and to apply successfully the accumulated experience of science. To achieve this aim, the courses of instruction must be carefully planned. In effect, a preliminary analysis must be made of the objectives and the means of achieving them.

One of the prime means is the lecture course, since this allows the presentation, in logical sequence, of the fundamentals, abstracted by the lecturer from his own knowledge and from the specialist texts (which are themselves not of direct use to the beginner, because they usually contain so many detailed illustrations that he cannot decide what is important and what is not).

There are several important ingredients of a good lecture course, and careful attention must be paid to each in its preparation [4]: they are (a) the subject matter to be included; (b) the organization of the subject matter; (c) the words used in presenting the material; (d) the use of audio-visual aids, such as the blackboard, slides, television and the public address system; (e) the delivery of the lecture; (f) the effective use of the voice.

The lectures must be supplemented by the reading of books, especially in chemistry, but as hinted above, the student must learn *how* to use such reading to best effect, and how to use efficiently the informational material in the library. Lectures should preferably be illustrated by demonstration experiments to underline important points and familiarize students with chemicals and technical expertise. Such experiments also provide natural breaks in the lecture to ensure that the student's attention is held. The lectures must also be related to the experiments in the practical course. The student must understand the importance

of basing practice on proper understanding and knowledge of theory and fundamental facts, whether in connection with the simplest titration or the most modern instrumentation, including the function of the components, maintenance of instruments, computer treatment of data, and computer-controlled experiments. At the same time, the experiments done should be related to everyday practice and the needs of industry and research, and coupled with an appropriate background in materials science to show the relevance of the analysis. Above all, the practical work should give the student a degree of confidence in his own manipulative skill and the validity of properly obtained analytical results. It is often instructive to include experiments in which the student deliberately uses incorrect conditions to discover what their effect is, and to learn how to devise simple tests for discovering whether gross manipulative errors have occurred. This assists in emphasizing that "the analyst must assume the ultimate responsibility for the design of the experiment and the interpretation of results" [5].

Even though in the last decade there has been a great increase in the amount of instrumentation taught in the laboratory, there are many combined techniques such as gas chromatography/mass spectrometry which involve expensive and specialized equipment, and though they have high informational content (both in terms of results and of education) such techniques are probably best dealt with in lectures and visits to research or industrial laboratories where they can be seen in 'real life' use. The modern emphasis on use of instrumentation must be coupled with a realistic appraisal of the performance and cost of instrumental methods in comparison with 'classical' methods, and hence it is essential not to exclude the study of reaction chemistry from the teaching process. Moreover, many instrumental techniques involve the use of reaction chemistry in the procedure and/or interpretation of results.

Belcher has well remarked: "Regardless of the advance of instrumentation, some pure reaction chemistry should still be included and lectures on sensitivity, selectivity, masking and de-masking, amplification, catalytic reactions, induced reactions, etc., cannot be without benefit" [6].

Another important factor in teaching analytical chemistry is persuading students of the necessity to study the historical evolution of the subject.

Szabadváry [7], an expert in the history of chemistry in general, and of analytical chemistry in particular, remarks: "However, it is becoming increasingly clear that the future development of science and technology cannot be judged or predicted without a profound knowledge of their past development, and there is no starting point for such extrapolation other than the path that they have followed to the present date".

Thus the lecture must present the general principle and development of analytical chemistry and chemical analysis, as well as the interface with other sciences. At the same time it must be clearly shown that the theory is not introduced for its own sake or to make the course 'difficult', but because without its proper understanding and use the results obtained may be incorrect, and

obtaining results that are as close to the truth as possible is the main concern of the analyst.

Ideally, the lectures should lead the student to see for himself the implications of each step, so that he can predict the next and enjoy the intellectual satisfaction of hearing his prediction confirmed. In this way he can be stimulated to think for himself and to recapture the joy of discovery felt by the pioneers. He must learn to use his mind to explore what to him is the unknown; he must become educated. Such a process is not easy. Most teachers would echo the words of Edison: "There is no expedient to which the human mind will not turn, to avoid the sheer hard labour of thinking".

When Philip West received the Fisher Award, he said [8]: "Why not products without chemicals when I see so many chemistry courses that have been purified to the point they too are free from chemical taint?", and further: "There is no quick way to become a chemist. Simply reading books and learning chemical theories can no more produce a true chemist than learning the theory of music can produce a real musician". If he had been Russian instead of American he would have summed this up in the well-known dictum "Theory without practice is sterile".

To become a true chemist it is necessary to have insight and intuition (a 'feeling' for the subject) as well as extensive knowledge of theory and practical experience of research. Only in this way can the chemist be able fully to understand the book texts, interpret apparently unrelated facts, and draw useful and interesting conclusions from them. The true test of knowledge and understanding (as opposed to mere recognition of phrases and ideas) is the ability to *apply* what has been learnt, to solve problems and explain new observations.

The history of the great scientific discoveries shows that these were made by scientists who deeply understood the aim of the research and worked enthusiastically and passionately for its achievement. In research in analytical chemistry the aim should always be to achieve the simplest and most accurate solution to the problem of measurement or identification that has been posed to the researcher, and in the framework of modern technology this is likely to involve the worker in interdisciplinary research and use of techniques originated in a variety of scientific fields. Hence the statement "The analytical chemist properly serves his role as a chemical measurements specialist only if he is a full partner in the interdisciplinary team concerned with solving the problem" [9].

The future analyst must, even as a student, learn to be a scientist, to be creative. The first and most important characteristic of a creative person is interest, and confidence is a close second. Lack of creativity is characterized chiefly by an incapacity or disinclination to become interested. Interest and confidence are closely interrelated and, normally, a sufficiently powerful interest generates confidence.

The problem for the educator, then, would appear to break down into the following parts [10].

- "(1) Ability to create or enhance an interest on the part of the student.
- (2) Steering the student to real unsolved problems which he is capable of solving to build confidence.
- (3) Possessing sufficient knowledge of the associated subject matter to answer questions and to properly refer the student to appropriate references.
- (4) Supplying to the student sufficient opportunity for the fundamental understanding of nature, that he may develop an appropriately sensitive filter to screen out bad ideas and pass on good ones".

A good teacher must finally show to his students some of the present limits of the science or equipment concerned.

Let us take as an example three of the most important parameters of analytical equipment: sensitivity, selectivity and rapidity in the transmission of analytical information. Even the best and most modern methods and apparatus are sometimes far from giving the performances achieved by systems in nature.

With regard to sensitivity, the most sensitive methods (such as neutron activation, electron microprobe, flameless atomic absorption) attain sensitivities of  $10^{-12}$ - $10^{-16}$  g. which may be compared with that of olfaction (smell),  $10^{-18}$  g. A recent paper on catalytic oxidation of aromatic amines, based its application to the complexometric titration of manganese(II) on olfactory indication of the equivalence point [11].

With regard to selectivity, the spider gives a differentiating response to certain alkaloids (caffeine, strychnine, morphine), the pattern of its web being altered according to alkaloid ingested. Another example of particular interest is the albatross, the only terrestrial being which drinks sea-water. It has a gland in its beak which instantaneously fixes the sea salts, the water becoming in this way fit to drink. The salts are then quickly removed. This natural mechanism is the envy of those working on ion-exchange processes for concentration or separation [12]. Recently [13] a new potentiometric sensor was based on coupling intact micro-organisms (*Streptococcus faecium*) with an ammonia gas-sensing membrane electrode. This bio-selective membrane electrode prepared with living bacterial cells provided a specific and linear response to L-arginine over the concentration range  $5 \times 10^{-5}$ - $1 \times 10^{-3}$  M.

The interdisciplinary nature of modern analytical chemistry is well attested by the award of half the 1977 Nobel Prize in Physiology and Medicine to Dr Rosalyn S. Yalow for work on the development of the technique of radioimmunoassay [14].

Analytical chemistry, in the last few years, has progressed almost into the realm of the imaginings of the science fiction writers, mainly by dint of fundamental research on analytical processes themselves, and on automation and computerization. The development of telemetry in connection with space exploration has revolutionized our ideas on terrestrial exploration for natural resources. The automated X-ray fluorescence analyser and gas chromatography/mass spectrometry were two of the stars of the 1976 Viking mission for the exploration

of Mars [15]. Every advance in technology brings a new challenge for the analyst. As the technological age is likely to continue in more or less its present form until man destroys himself or reaches a level of social and political wisdom approaching his level of scientific knowledge, there will be a continuing need for analysts. It is the duty of teachers and educators to see that the future generations are properly equipped for their task.

# Teaching and Education in Chemistry

---

## 1.1 TEACHING VERSUS EDUCATION

Teaching does not always give culture, but frequently the contents to a culture [16].

An old parrot cannot learn to talk [17] (Bengalese saying)

We shall try to discuss logically and critically the problem of teaching versus education in chemistry. This question may be universally debated but it is the unfortunate state of affairs that few chemistry teachers in universities know, or wish to know, the difference between teaching and education, or even realize that a difference exists.

Berrell has said “A great teacher is not simply one who imparts knowledge to his students but is one who awakens their interest in the subject and makes them eager to pursue it for themselves. An outstanding teacher is a spark plug, not a fuel line” [18]. In other words, a great teacher is an educator (in the sense indicated in the introduction). It follows that greater emphasis must be placed on the quality of teaching, particularly at the undergraduate level, and the rewards for outstanding teaching must be put on a par with the rewards for outstanding research. To be a good teacher and also a good research worker is the ideal, and may not always be realized.

To teach in a scientific field and to continue learning, it is necessary to know the history and evolution of the subject, because there is no progress without knowledge of the past and present. Moreover, anyone failing to continue to learn (especially from the difficulties experienced by students) is not entitled to be called a teacher.

There are two deeply entrenched traditions relating history and the sciences: one in which the history of science is connected with historical studies in departments of history, the other in which the histories of the special sciences arise from within the sciences themselves and remain centred in scientific departments [19]. It is necessary, however, to remember that the history of science is not a substitute for science itself.

For these reasons teaching in chemistry must include a general but concise

history of chemistry, and each specialized course in the different branches of chemistry should contain the appropriate historical facts, preferably enlivened by brief anecdotes about the persons concerned, and related to the general cultural background of the period. Present-day students are often glad to be informed of the precedent of Mendeleev having his hair cut only once a year (on his birthday) or of the Pauli effect on apparatus\* or that Rayleigh was obliged to ask his assistant to remove her corset (which had steel stays) before helping with his magnetometer experiments.

The history of chemistry is sufficiently important not to be left solely to retired professors or to the weekend activities of interested chemists, and should be dealt with by specialists. According to Ihde [20] a good history of chemistry course should have the following features.

(1) Integration of the several traditional branches of chemistry into a coherent whole.

(2) Creation of a realistic picture of the science, showing that chemistry is a dynamic rather than a static subject.

(3) Putting chemistry into perspective as a human activity.

To know the history of chemistry in general and that of analytical chemistry in particular is a prerequisite for a teacher or research worker in analytical chemistry. Only in this way can chemical initiative and creativity, without fear of mere rediscovery, be ensured. Only a scientist having adequate knowledge of the history of science, both past and present, can understand the status of the science, adapt to it and pursue research constructively and usefully, producing innovation and development. All too often, so-called research consists of treading well-worn paths, and producing insignificant variations on long-known techniques, or even methods that are inferior to those already in use.

Kunin [21] in his book on ion-exchange resins gives an excellent and concise history of ion-exchange, exemplifying the precept that in any historical treatment unusual excerpts should be given to stimulate curiosity and awaken scientific thinking. It is often difficult, for example, to decide who originated a certain technique or how it has been developed. Thus Kunin remarks "A recent interpretation of the miracle supposedly performed by Moses as he led the Israelites safely through the wilderness suggests the possibility of the application of ion exchange. In order to make the 'bitter' water at Marah potable during their journey, Moses found a tree 'which when he had cast it into the waters, the waters were made sweet'. It has been suggested that the oxidized cellulose of the tree entered into an exchange reaction with the bitter electrolytes of the water, rendering the water potable". Curiously, no-one seems to have tried to repeat the work and identify the tree or the water. We offer this as a research 'project' for anyone so bereft of ideas as to need it.

\* Pauli's presence was reputed to cause apparatus to cease functioning, the extreme case being facetious attribution of a failure to the fact that Pauli had passed through the town in a night-train.

To conclude, we may say that the history of science constitutes the connecting line between teaching and education, since it can use the first to produce (or induce) the second. It follows that ideally the teacher of chemistry should have a good knowledge of its history.

Fundamentally, a university preserves, interprets and extends human knowledge [22]. The university teacher is expected to participate in all three activities. Thus he is required to be a good research worker, who uses the results of research in his teaching, to arouse the interest of the student, but his teaching only becomes active if his students are an active and creative element in it; in other words, if the students really want to learn, and hence begin to teach themselves. The information given through lectures constitutes only an 'activation' step for the students, awakening their curiosity and inviting them to the library, where they begin to learn the 'art' of learning, through the use of textbooks. It is clear that the textbook is one of the most important vehicles used in learning and teaching chemistry [23].

If the teaching is good, and the student uses good and attractive books, he may reach the second part of the learning process, which is education in chemistry. To achieve this, the student must, at least in the first stage of learning, make efforts, sometimes unpleasant, to accumulate knowledge. This is because the very essence of science is the imposition of order on the chaos of sense impressions and data received from the physical universe. That is to say, the progress of science produces a decrease in entropy, and hence involves a loss of free energy. The energy required must be supplied by the scientist (or, in the case of learning and education, by both the teacher and the student).

Research work in every field of science is nowadays largely based on application and interpretation of knowledge judiciously selected from the enormous amount of information (some good, some bad!) available in the modern literature.

The student, or a beginner in research work, must act as a filter, selecting logically and critically (and retaining) the necessary knowledge. He must learn to retain not only the essence of what he has read but also any subsidiary theoretical or experimental details which may be of use as the starting point for future investigations or in their realization in practice.

The mind of the research worker in chemistry must sift out the useful knowledge and eliminate the useless, just as the flamingo feeds itself from silt, retaining only the food contained in it [24].

We insist upon the importance of filtration of information and upon the role played by the teacher in guiding the student to learn how to achieve it. It is nowadays almost impossible to cover exhaustively even a strictly specialized domain of a science, whatever method of information retrieval is used, and it is necessary to learn how to abstract rapidly and accurately the essentials of the most important work. This involves a value judgement, and the student should be taught to read scientific papers critically (as a referee does) [25], so that he is not deceived by specious and incorrect work that has escaped detection before

publication. During the writing of this book, it became abundantly obvious that the literature contains too much poorly written, poorly edited and inadequately proof-read material for comfort, and that the reader must always be on guard and act as an additional referee. This does not make it any easier for the student (especially the beginner) to use the literature!

We now reach the second stage of the learning process, namely the active work of a student or research worker in the laboratory. The laboratory phase follows logically after the informational phase, in order to ensure correctness in the work and the interpretation of the results. There are, unfortunately, some otherwise good chemists who neglect in their work any previous and sound observations on their research problem. They can be likened to a virtuoso violinist who does not take the trouble to learn to play the correct notes. They are at most technicians, but not research workers.

It is important to teach students to make their own observations, describe them accurately, draw independent inferences, act on them, and accept proof or disproof of the inferences [26].

We may conclude that teaching and education are interactive and inter-dependent. Teaching is necessary (but not sufficient) for education, and vice versa. Teaching points the way to education, but really the successful student educates himself in the sense of learning to apply his knowledge to solve problems and to perceive the inter-relationships in science and nature.

It is not everyone who is capable of teaching, especially science. "Teaching is more than a science and more than an art. It is both. Those of us who teach science are lucky in that we can use all the artistry available to our colleagues outside science, and our training enables us also to use science more easily and more efficiently. ... Successful teachers owe much of their effectiveness to experience, dedication, and a natural gift, but it is also clear that a scientific and practical approach can augment these characteristics. Teaching requires creativity and innovation in both the scientific and artistic senses" [27].

There is an intimate dependence between the teaching process and education. It is often the case that the two processes cannot be distinguished from one another, and even specialists sometimes mistake the one for the other.

One of the difficulties is that most systems involve teaching by a large number of specialists, with the result that there is no overall co-ordination, and instead of learning a single subject or discipline (chemistry) the student feels he is learning a large number of totally unrelated subjects, and becomes not only inadequately educated but also disenchanted with chemistry.

A more satisfactory state of things may be found in the Japanese learning system. "The heart of the educational system at the major Japanese universities is the organizational unit termed the 'Koza', which stands for the research teaching group associated with the laboratory of each full professor" [28]. This may be regarded as a development of the old method of teaching by 'regents' in the ancient Scottish universities, in which each regent was responsible for the *entire* education of a group of students.

## 1.2 TEACHING CHEMISTRY

"Chemistry has for its object mixed bodies, insofar as they are divisible and soluble, upon which it works so as to extract from them the *trois Principes* (Basic Elements), which are Salt, Sulfur, and Mercury; which is done by two general operations, namely Solution and congelation" [29, 30]

What should be taught in chemistry courses today? It is certain that every chemistry teacher has asked this question of himself and of others.

The first essential is that the teaching of classical and modern ideas of chemistry should not be diluted; it should be strengthened [31], so that irrespective of whether the student wants to become an industrial chemist or to do research in chemistry or to be a salesman for a chemical company, he will be aware of the structure, methods and purpose of the subject. Thus the definition of chemistry itself must be adjusted to be in accord with the stage of development of the science, especially in view of the rapid developments in chemical research.

We consider a correct definition of chemistry in its present status of development might be: "Chemistry is the integrated study of the preparation, properties, structure and reactions of the chemical elements and their compounds, and of the systems which they form" [32].

We consider that on this definition chemistry may be tackled by any person having sufficient intellectual aptitude and interest.

Dr Jacqueline Renaud says [33] "The new schools of neurophysiology have ended with the 'gained facts' defended by the old phrenologists: for example, the intelligence quotient does not depend on the amount of grey matter or the dolphin would be more intelligent than us. The dynamic study of the brain deals specially with the links between neurons. Those links make possible the act of learning, in other words, education".

The thing that becomes clear from its definition is that chemistry, more than other sciences, has developed in close relation to technology. Therefore chemists tend more toward practical applications than do other scientists. Through the years of the great developments in the sciences, biology, physics, mathematics and astronomy have had their centres in academic life and have been largely the preserve of academics. Chemists, on the contrary, have felt more closely tied to industry, even those chemists who are primarily academics [34].

This observation is now rather less generally valid, since many of its academic teachers (other than analytical chemists) tend to regard chemistry as a 'pure' science which should be kept separate from its numerous technological applications, such as industrial chemistry and chemical engineering.

This is our starting point. We must now see *how, by whom, to whom and under which conditions* chemistry may be taught.

### (a) *How*

Chemistry is taught to two general audiences, the intending chemists and those who are required to study chemistry as an ancillary subject. The teaching in the two cases should be different, but it must not be forgotten that teaching

in any scientific field implies the selection of information from the continually growing amount available, and the desire to introduce the latest ideas to show how 'advanced' the teacher is may result in either omission of more important 'old' material or the coverage throughout the course being rather superficial. The answer is simple: teach the fundamentals first. If these are properly understood, the 'new' material will be easier to teach and more easily grasped. It must be remembered that in a given time only a certain amount of information can be presented to and taken in by the human mind. This amount of material can be thought of as three-dimensional: if it is deep, it must necessarily be based on a very small area; if it covers a wide field, it must do so in a very shallow manner.

It is therefore necessary to take into account the nature of the students' pre-university schooling and to balance carefully the weight given to the different branches of chemistry. It often happens, for obscure or subjective and sometimes untenable reasons, that the importance of one of the chemical disciplines is undesirably diminished or overestimated. A notorious example is the pseudo-scientific competition between inorganic chemistry and chemical physics on the one hand and analytical chemistry on the other, as a result of which, analytical chemistry is the Cinderella of chemistry in many European countries, as demonstrated by the small numbers of independent departments of analytical chemistry in those countries, especially in Great Britain. It is not enough simply to appoint professors in the subject: the subject itself must be recognized as being just as important as organic, physical and inorganic chemistry, and until it is given adequate teaching time and facilities, industry and research will continue to be hampered by a lack of properly trained analytical chemists.

Torrey remarks [35] that "Too often analytical chemistry is taught as if it were an abbreviated orientation course for technicians, in that the students are instructed to 'flip' switches and be 'black-box' operators instead of students of Chemistry". The courses must be taught by experienced and enthusiastic analytical chemists who have the necessary background knowledge to put the subject into perspective and show its relationship to the other branches of chemistry. Analytical chemistry is the only branch of chemistry which brings together all three other branches and uses them for practical problem solving. It would be quite possible to construct an entire chemistry course based on analytical chemistry, with the teaching of organic, physical and inorganic chemistry geared to their relevance to the analytical course, but to do so would be no sounder, in terms of training, than the present system in which analysis may scarcely be mentioned at all. It is ironic that Ostwald, who first put analysis on a sound theoretical basis, should have been responsible to some extent for the present state of affairs, with his observation that "analytical chemistry plays the role of a servant to other sciences, being at the same time subordinate but also indispensable". He forgot that without analysis chemistry could not have existed as a science.

Given that a proper balance can be achieved between the subjects, the question of technique in teaching remains. Teachers now have available to them a series of 'aids' to teaching (audio-visual presentation, computers, etc.) but the efficiency of these depends on who uses them, how, and for what purpose. To give an example, there are now available various lectures on instrumental analysis, recorded on audio cassette and illustrated with slides. This kind of lecture is very useful for individual instruction or for people who wish to know about a certain type of instrumental analysis, but it cannot always be an adequate substitute for the traditional lecture course, which can be interactive between lecturer and audience. The specialists or professors cannot be replaced by information-transmitting machines, however 'intelligent' these machines may be.

Brasted [36] remarks "I would hope I could in the lecture atmosphere transfer something of what might contribute to education better than by using an audio cassette, taped TV lectures, or a computer".

A teacher who is active in research and abreast of developments in his field can inspire students with his own passion for scientific research, including in lectures his own experiences and showing the relationship between research work and the practical problems and needs that gave rise to it, and how the difficulties were recognized and overcome. In this way the student is led to feel in the vanguard of science.

Anyone aspiring to teach chemistry successfully must strike a proper balance between theoretical and descriptive chemistry, and must never lose sight of the fact that chemistry is a *practical* science, and without its technological and economic aspects is only slightly more useful to mankind in general than the study of the sex-life of the dodo. The days of the notion that *any* extension of science is its own justification (irrespective of its real utility) are long since gone, though even a cursory glance at the research literature will show that a great many 'researchers' have not realized it. The teacher should endeavour to put chemistry in proper perspective for the student, and train him to consider the facts for themselves, stripped of the sophistry of words that seek to vest them with undue importance [37].

Thus Hutchinson [38] remarks: "I am seriously concerned that many of today's students are so deficient in the vocabulary of concrete chemical reality that, for example, they neither know nor particularly care to know the empirical facts of inorganic chemistry or the treatment of the raw materials on which our nation's bountiful economy depends".

#### (b) *By whom*

Science can be taught successfully only by those who are thoroughly versed in it and captivated by the spirit of science and scientific research. In Section 1.1 we expressed the opinion that a good teacher will also be a good research worker. Some people hold that a bad teacher may be a good research worker and a bad researcher a good teacher, but the second view is like saying that a music teacher

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need not be able to sing or play an instrument. As for the first, the most that can be said in its favour is that a bad teacher acts as a sorting mechanism, the good students turning to the library to remedy the effects of his deficiencies, and the poor students being even more retarded than they are already. For the teacher to act as a catalyst in the awakening of the student's interest in science, he must spend many hours working in the laboratory and library to become a part, however humble, of the progress in his chosen field.

Libby says [39] "It is, therefore, of extreme importance that we improve scientific education by helping the teachers not only at the college but also at the high school level to impart the excitement of chemistry and science in general so that the value of science, and chemistry in particular, can be transmitted to their precious young charges.

To be absolutely honest and practical we must try to interest the young student in science, and chemistry in particular, by showing him the excitement and wonderful thrill of discovery itself".

Such discussion of new scientific results, appropriately selected, is of special worth. The student can in this way be stimulated to educate himself by working in library and laboratory. A lecture has attained its goal if the students talk about its topic afterwards.

### (c) *To whom*

According to Mészáros [40] students should not be classified simply as mediocre or outstanding, but several categories should be used, as follows.

"Student talented for leadership, with great self-reliance  
 Excellent co-worker under proper guidance  
 Adequate co-worker when led properly  
 Stubborn, willful or obstinate student who cannot be led  
 Student without any initiative or self-reliance, who cannot be led."

This classification helps the teacher to know the human material with which he must work and to know in what directions the future graduate may be guided for his benefit. It also helps in discovering the true talent amongst the students, from which future research workers can be drawn to ensure continuity and novelty in the work.

The students themselves are often the best judge of a teacher, since they are usually the only people who hear what the lecturer has to say (though some lecturers are inaudible beyond the first two or three rows of seats) and know whether his style is easy or difficult to follow, whether his lectures are lucid or not, whether he is dull or interesting, and so on. For these reasons it is often recommended that students should be asked to complete questionnaires about their teachers. A typical questionnaire [41] asks the students to give their responses to the following statements.

**The teacher**

- (1) is always well prepared
- (2) makes good use of class time
- (3) has stimulated my interest in the subject area
- (4) expects that much time and effort be given to the course outside of class
- (5) is interested in the student's progress and is actively helpful
- (6) is effective

The responses (to be indicated by insertion of a number of symbol) are to be chosen from: strongly agree, agree, neither disagree nor agree, disagree, strongly disagree, have no opinion. Whether the statements are the best to use is another matter. The value of such questionnaires is open to question, however, since the student sense of humour (especially in Great Britain) may make the results worthless. Moreover, not every student is a good judge; a student may be so incompetent himself that he has no feeling or perception for competence in others.

**(d) Under which conditions**

This problem is not new, but is still with us, and likely to remain for a long time to come.

In ancient times a student who wanted to learn went to a teacher, studied with him until he was satisfied, and then left to use his learning [42]. This led to the celebrated science schools (or chemistry schools), existent in the past in some European universities and at present in Europe, the U.S.A. and Japan.

The existence of a renowned chemistry school depends to a large extent on the head of the department, who ensures good facilities and a good atmosphere for the work of a team, and the continuity and tradition of the scientific activity.

A favourable climate for scientific research may stimulate multidisciplinary lectures such as chemistry-physics, biology-physics, biology-chemistry [43]. These lectures are useful for future college teachers and may also ensure the production of good specialists in interdisciplinary fields. This interpenetration of disciplines is essential for cross-fertilization of ideas, and for successful work in the boundary areas. We would not think of a biochemist as a 'good' one if his knowledge of biology and chemistry was kept in separate compartments in his mind, just as we would not speak of a good biophysicist if he knew physics but not biology (or vice versa).

In this domain of interdisciplinary research teaching promotes only the spark, the torch being kept alight, as we shall see later, by education.

Multidisciplinary teaching—like multidisciplinary research—calls for scientists more broadly trained than the run of the mill. The unity of science itself is evoking counterparts in unity of teaching and unity in research [43].

### 1.3 EDUCATION IN CHEMISTRY

Chemistry is questioning nature, questioning fellow chemists [44]

As we have tried to show, there is a difference between teaching a scientific discipline and education in and through this discipline.

Education in chemistry or other domains of science involves a series of interdependent constituents. Our experience as teachers and research workers leads us to conclude that the principal components of education in chemistry are:

- (a) printed lectures or textbooks;
- (b) reviews and journal articles;
- (c) individual or team research;
- (d) direct relations with other specialists and participation in conferences or symposia.

Let us consider these in detail.

#### (a) *Printed lectures or textbooks*

These supplement the knowledge received directly from lectures but cannot alone form an adequate substitute, since the essence of the lecture course is to select the basic material from such sources and put it together in a logical progression to form a satisfactory and self-contained whole.

There is an essential difference between printed lectures and textbooks, which is obvious to any beginner in study of the field concerned. The goal of a printed course is to ensure provision of useful material to the student, as a second form of information on the topics of the lectures. To reach this goal, the printed course must contain theoretical knowledge tied to descriptive matter to supplement the lecture material but with only a limited proportion of explanatory text. Courses that are strongly theoretical in character, such as chemical physics, must avoid complicated mathematical derivations in lectures in order not to obscure the physical meaning of the phenomena, and the printed material is the proper place for such mathematical exercises. Such printed lectures are quite efficient if they are strictly confined to the topics necessary for the student to assimilate the fundamentals of a subject. Otherwise the student must guess which material is useful and may not be able to differentiate between fundamental essential topics and supplementary ones. Collections of such printed lectures should not be too lengthy. Their main value is perhaps that the student is no longer in danger of having incorrectly taken lecture notes (or can at any rate check them) but against this must be set the loss of practice in note-taking, if the student decides to rely entirely on the printed lectures.

We must not confuse a printed course with a textbook, even an 'elementary' one, since such texts usually give the student much more than is necessary for his stage of learning. The value of a course is due to the quality and not the quantity of informational material presented. A telephone directory has a very high informational content, but is not very educational!

To present in a printed course only the necessary fundamentals means that the author must have a very wide background of reading and a profound understanding of both the subject itself and the difficulties likely to be experienced by the beginner in learning to understand. Almost every chemistry department will have on its staff a teacher who gives lectures which are models of clarity and organization but are extremely difficult for students because the teacher makes no allowance for the fact that the students do not possess the teacher's background knowledge, and fails to put the topic into terms that *are* familiar to the students and that they can understand.

Many authors of chemistry textbooks seem convinced that a maximum of theorization is the best answer to the students' requirements. There are, unfortunately, some chemistry texts from which we cannot guess where the knowledge of chemistry begins or ends.

There are some who hold that it is possible to be a good lecturer without necessarily being able to write a good textbook. This seems unjustifiable as a generalization, because to teach means to understand, and to understand means to be able to apply what has been learnt. Whoever can do that, can equally well write out his lectures and have them printed. Besides giving the student an accurate set of notes, such printed lectures can stimulate the student, arouse his curiosity, and lead him to understand the importance of textbooks as an aid to putting factual flesh on the bones of the subject given in the lectures, and to seeing how the ripples of knowledge spread outward into the unknown. The textbooks the student will meet at this stage will be 'intermediate' textbooks which provide material to be learned and also orient the student towards other books and papers in the specialized literature.

These 'intermediate' books should not exceed say 300 pages, and should contain judiciously selected material and problems, and practical exercises if experimental techniques are described. It is recommended that such books should be designed on the American pattern, having a moderate amount of theory and the subjects being amply illustrated with pictures, tables, diagrams, etc. We give as an example Parikh's book on absorption spectroscopy of organic molecules [45]. This book attains the goal proposed, and is very useful for students studying organic chemistry. It presents in an original manner the main spectral techniques for investigation of organic compounds and shows the correlation between the methods. Examples and exercises are given in order to familiarize the student with the infrared and nuclear magnetic resonance techniques. We feel it can be taken as model of its kind.

The third category of books comprises the specialist texts, which may be divided into (a) treatises, (b) monographs, (c) strictly specialized books.

Treatises are useful only up to a certain point, and their advantages are sometimes outweighed by their disadvantages. They contain a tremendous amount of facts, but in comparison with monographs treat the facts rather superficially. Moreover, if they have many volumes, the earliest will often be out

of date long before the last have appeared, and if a particular volume has many authors, one or more of whom may be much slower than the rest, some chapters will also be outdated when the volume appears, and subsequent volumes will be delayed if the publication schedule calls for rigid adherence to a structured plan.

A good treatise should be written by a team of specialists, the duty of the editor being to select the team and to arrange the material. The editor must be firm, however, and not allow the over-enthusiasm of an author to lead to an imbalance. We consider that the role of the editor is of extreme importance, like that of the manager of a research team in work of complex character. Owing to the international character of research, the most efficient are treatises written by teams formed from authors belonging to different nations.

Monographs are books which contribute, together with journal articles, to exhaustive documentation in a field of science. They should be written by research workers with rich experience in their field, and who are meticulous and correct in the selection of material. As informational sources, monographs play an essential role in the educational process. There are several series of very good monographs produced mainly in America, Great Britain and Germany.

The strictly specialized books are akin to monographs but in a very narrow field, written for advanced and 'superspecialized' research workers. They are of special interest but limited use. We give as examples: *The Analysis of Rocket Propellants* [46] and *Analytical Biochemistry of Insects* [47].

### (b) *Reviews and journal articles*

An important part in any science is study of the literature, since this is the printed record of the development of the subject. The specialist should read an article directly in the original journal (if he knows the language) and not just its abstract in a documentation journal such as *Chemical Abstracts*. The abstracts are useful for rapid exploration and orientation, and as a 'lead-in' to the literature on a subject, but are an inadequate substitute for the original papers when detail is necessary. They are not always accurate, and their usefulness is largely determined by the efficiency of their indexing and the ability of the reader to use the index to maximum benefit. The original paper may also contain useful ancillary information that is not abstracted, but may be of great use to the reader.

The reading of original papers in journals constitutes a relation of the research worker to the thinking of other people, the first step toward co-operation between specialists. There are numerous cases where fruitful co-operative research has been initiated in this way.

Depending on his interests, the research chemist should select a number of appropriate journals (usually between 15 and 20 will suffice) which he should consult as they appear. For rapid coverage of other journals he can consult informational publications such as *Current Contents*. In spite of the continuously

growing amount of information published, we are convinced that a competent chemist can easily select the most important articles in his field.

Computerized storage, search and retrieval methods are often advocated as superior to the 'old-fashioned' personal search. Computer searches can indeed be very rapid and efficient, but much care in the planning of a search is needed to ensure that all relevant material is retrieved, and to avoid recovery of large amounts of irrelevant material. Their efficiency often depends on the initial subjective choice of key words stored, the 'early' literature (pre-1967) cannot at present be accessed, and they cannot make value judgements.

Another important means of documentation, somewhat similar to monographs, is the review. If well written, reviews constitute an ideal source of information, but it is essential that they should be *critical* and not mere catalogues. As a certain book review once put it, academics are expected to keep card-indexes, but not to publish them. Most major journals publish review articles from time to time, and *Analytical Chemistry* publishes every April a special number consisting exclusively of reviews of selected topics, fundamental and applied research being dealt with in alternate years (even and odd respectively).

### (c) Individual or team research

Another component in the education of a specialist is his laboratory work. It ensures contact with colleagues and, in the first stages of the work, with the leader of a research programme. The work may be done by an individual (e.g. for a Ph.D), or by a team. In team work, the working atmosphere plays a special role, and a prerequisite for a successful research school is a climate favourable to research. The age of the 'ivory tower' is now past, and has been replaced by the age of 'active research', which means work in the team and for the team.

For scientific research in general, the questions 'on what?' 'how?' 'what for?' and 'by whom?' are ever present.

Let us briefly examine the answers.

#### *What?*

Traditionally, in principle anything may be investigated, in scientific research there being only major or minor problems. There is sometimes a reversible equilibrium between them. We can give as an example the study of the rare-earth elements and their compounds. In the early history of chemistry, this was considered as a curiosity, these elements being looked on as a series of chemical elements that were very similar, difficult to separate and of no use. For students studying inorganic chemistry they later constituted only a nuisance, the students being obliged to memorize a lot of things judged as of very minor importance. As a result of the development of improved techniques of separation, such as solvent extraction and ion-exchange chromatography, however, the lanthanides and their compounds may be obtained very pure, and their chemistry has become

of major importance, especially since new technological applications have been found, in colour television for example.

In practice, however, there is a growing feeling that the relative importance of a line of research *can* be assessed and applied in choosing *what* to do research on. In our opinion, for *training* in research methods, e.g. for a Ph.D., the main factors in the choice of a topic are that the subject should be of interest to both the student and the supervisor (to ensure enthusiasm and the continuity of a line of work), that the work can be completed in the time available, and that the topic is suited to the ability of the student. There is little point in asking a mediocre student to undertake a highly problematic and challenging problem, or a brilliant researcher to undertake a trivial 'number-finding' exercise. Both students would feel frustrated, though for different reasons.

The topic should also have *some* relevance, however small, to the needs of the world. Far too many so-called research schools tread paths so well beaten that no initiative, insight or inventiveness is needed to obtain results (which will duly be published and add yet another useless bit of information to the literature).

The days when *any* bit of new information could be treasured for the sake of its novelty alone, and stored away in case it *might* be of use in the future, are long gone. If our critical faculties have not developed to the extent that we can differentiate between work done for a specific use or purpose and work of the 'number of angels on the point of a pin' variety, the centuries of patient endeavour have been in vain. What is more, the politicians who fail to see that the world situation demands the organization and mobilization of all available scientific resources to solve the fundamental problems of energy and food supply and overpopulation, or to take action if they do see it, are not only behaving like ostriches with their heads in the sand, but betraying the people they purport to serve. Enormous sums of money and amounts of energy are wasted on projects that are trivial in comparison with the problems that beset the everyday life of something like 90% of the world population, and about which nothing is done. Until we get statesmen instead of politicians as our rulers, nothing will be done until it is too late, so all we can hope for is that sufficient scientists will have the wisdom, foresight and courage to insist on usefulness as a criterion, and abandon the safe 'sausage-machine' type of research.

Any school of chemistry worthy of the name will have a tradition of work of outstanding importance, a tradition that must be maintained. Such research schools foster international collaboration, young people of all nations seeking to take research degrees in them, attracted by their research activities and renown. The future is in the hands of these research schools and the workers they produce. These workers will be those selected for the team work that is necessary for the solution of the long-term and difficult research problems such as exploration of ideas for new techniques, examination of mechanisms, development of new instrumentation, solution of hitherto intractable problems. This kind of research is most suitable for post-doctoral work, the Ph.D. training being an intermediate stage between undergraduate studies and true advanced research.

As Wotiz [48] has remarked, in some countries the Ph.D. degree is not awarded until the recipients are in their mid-thirties, and another ten years or more of sustained research may be needed to obtain a D.Sc., whereas American or British universities will not hesitate to appoint to their full-time teaching staffs recent Ph.D. graduates, sometimes less than 25 years old.

Team work is best conducted with staff starting in their thirties, in order to have a young team, but this means that the Ph.D. should be obtainable by workers in their mid-twenties.

### *How?*

Any scientific research must start with a literature search, although some workers are said to advise students *not* to read anything on the subject, so that they do not start with preconceived ideas. Sometimes a computerized search may be made, but as already said, that presupposes that the relevant literature has been adequately abstracted and committed to computer memory.

For complex or interdisciplinary research, adequate equipment and resources must be available. Much modern research involving instrumentation may require a very large investment (with rapid depreciation) in equipment and materials. Nuclear reactors, for example, are extremely expensive (and unobtainable second-hand), and even a multichannel spectrometer may represent the lifetime income of a small tribal village in an underdeveloped country.

There are those who consider scientific research as a costly hobby. They are quite right if the research has no valid or perceptibly achievable objective in terms of global human needs. Even when the research *is* valid in these terms, and done with all thoroughness and conscientiousness, if it proves fruitless it has diverted money and effort from other work that could well have proved more beneficial. Unfortunately, research has come to be regarded as sacrosanct, although the triviality of much of it is at once obvious to an intelligent enquirer, and to question its aims and validity is treated as heresy.

Of course, this is not to deny that lack of adequate equipment and resources can hamper research work; the modest results in biochemistry in the past are an ample illustration of the point. We wish only to draw attention to the fact that science is often unscientific in that it fails to question itself, and that the channelling of funds into research seems to be as much a matter of fashion, self-esteem (and possibly self-interest?) as of objective appraisal of the likely worth of the results of the work.

### *What for?*

We cannot speak about a research without a purpose. Even alchemy had an aim, even though it proved chimerical. The main goal of scientific research is to make man free, i.e. to think freely, to improve his life and working conditions, and to ensure progress. A true scientist is a free man in the true sense of the words, because he possesses freedom of thought and audacity in investigation.

Science is traditionally international; it does not belong to one nation alone. It is erroneous to speak about secrets of research, because the results of a research may be found sooner or later by other scientists in various countries. To keep secret the results of a fundamental research merely delays the progress of science.

It is said "To know is to be strong". If a scientist becomes strong through knowledge, it is nonsense for him to fear that his research results may be stolen. This mentality of secrecy belongs to the past and the politicians (both scientific and non-scientific); the results of fundamental research are published and are rapidly known to all people working in that particular field. The only danger of having results stolen may arise during publication, if an unscrupulous referee delays a paper while pushing through a plagiaristic piece of work and claiming to have originated it, but such an action, once discovered, would completely discredit its perpetrator.

There is an indivisible connection between fundamental and applied research. Thus Laitinen [49] has commented "It is useful, perhaps, to remind ourselves that basic research is not synonymous with useless research. Rather, by its nature, it potentially is of broad, long-range significance. In contrast, applied research is potentially applicable in a short time, although its consequences are more narrow. The two are by no means incompatible. On the contrary, a mission-oriented research project would greatly benefit by a judicious flavoring of basic research". Unfortunately, the fallacy of the undistributed middle remains as potent as in Aristotle's day, and on the basis of a few examples of later important applications of what had originally been thought useless work, a mistaken belief has grown up that therefore *any* work is justifiable on the grounds that it may prove of immense value at some unspecified time in the future. We have already expressed our opinion of this specious argument (p. 28); in our experience there are extremely few beggars on horseback.\*

What Laitinen is saying is that any major step forward is based on a new interpretation of facts patiently accumulated by hard work, or on a new insight into the connection between the facts, but the facts themselves must have been intelligently selected in the first place. This is the nature of all advances in scientific theory [50]. The same holds for applied research: the problem must first be defined, and routes to a solution sought on the basis of experience and analogy. If one route fails, another must be tried. It is well known that the appearance of a new medicine on the market is preceded by a colossal amount of work, sometimes involving many years of research on thousands of compounds that have been synthesized and tested.

Organic synthesis, for example, can be likened to alpine climbing, in that the goal can be attempted by various routes, depending on the imagination or audacity of the team. The analogy can be completed if we suggest that the most efficient synthesis corresponds to the easiest route to the summit, but the

\*If wishes were horses, beggars would ride.

more difficult routes may give more insight into the means of solving the technical problems.

The most remarkable scientific results implicitly assume initiative, audacity and imagination on the part of the worker. Unfortunately the published results do not always reflect this, there being a modern tradition in scientific writing that such emotional aspects should be suppressed, though it was not always so in the past. Thus even papers of fundamental interest and importance may at first appear 'flat' and uninteresting to the reader, since they tend to be written in the same style as papers which may merely describe simple adaptations of methods or techniques (adaptations that are within the power of any competent technician). Fortunately it is not difficult to differentiate between them in terms of value.

Sanderson [51] has posed the provocative question "Can chemistry be learned without understanding?" and given the answer "... yes, if a chemist is a technician. The answer is no, if he is a scientist", but to us this seems to beg the question of what is meant by 'learning'. To us it *means* understanding, and Sanderson appears to confuse learning (which has several meanings) with Pavlovian response, or mechanical repetition. In our experience, technicians who do not understand the chemistry they are required to use are not much good as technicians anyway.

#### *With whom?*

We have already partly answered this question. It is clear that any suitably trained person can do scientific research, irrespective of its nature, but aptitudes and abilities vary, and the members of a research team should be chosen according to their skill in the particular complementary techniques needed. Thus there is "...the need for more effective utilization of human resources. This is a difficult, controversial area, but clearly real costs are incurred from misplaced, misdirected, under-utilized, and non-motivated employees" [52]. The research team should have proper proportions of research workers and technicians, depending on the character of the research. We give as illustration the organization of a research team at the Japanese Petrochemical Company Mitsui (Fig. 1.1).

Choosing the team for interdisciplinary or multidisciplinary research is rather difficult. Laitinen [54] says "A distinction is occasionally made between interdisciplinary and multidisciplinary programs according to whether experts from various departments are assembled into teams to seek solutions to specific problems or whether scholars from different disciplines share common research facilities to work on problems in the various fields". The best example is perhaps work on automation in analytical chemistry. The good analyst knows what kind of equipment is needed, but must participate in the construction of new devices, usually designed by mixed teams of specialists, chemists, electronic engineers, mathematicians, etc. [55]. The current interest in equipment based on use of microprocessors has resulted in evolution of a new breed of technologists, complete with a jargon of their own.

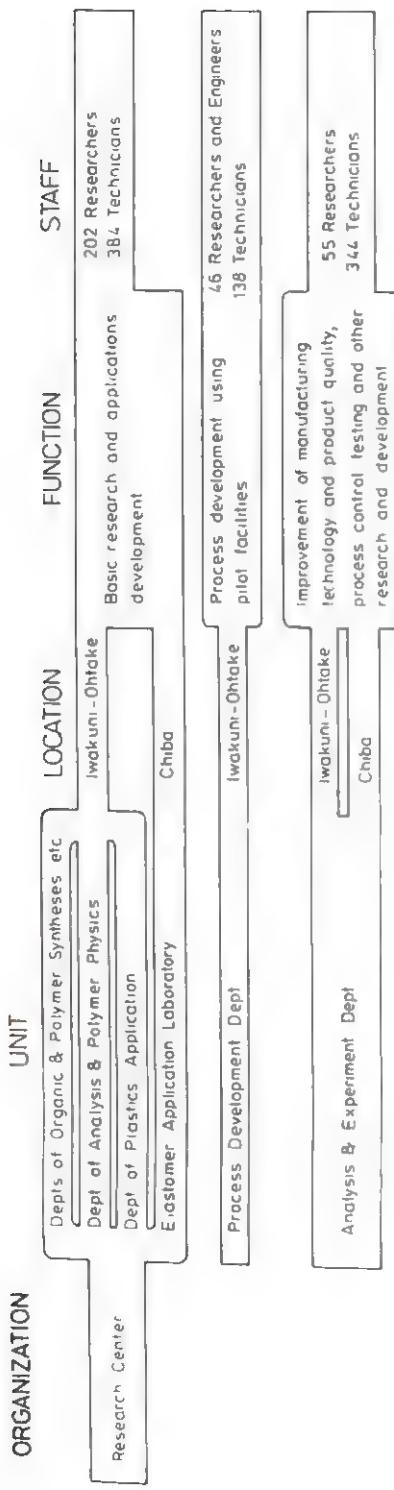


Fig. 1.1 Mitsui organizing scheme [53] (by courtesy of the Mitsui Company).

The use of microprocessors ensures rapidity and reliability in processing of results, and microprocessor-controlled research equipment is reaching a state of maturity and reliability adequate for it to be used by non-specialists unfamiliar with the details of its design and manufacture. Nevertheless, as is always the case with packaged instrumentation, the user is well advised to study the fundamental principles underlying the measurements he is making, in order to avoid nonsensical applications [56].

(d) *Direct relations with other specialists, participation in conferences or symposia*

We have already emphasised the international character of science. An important part in scientific education is the participation of the research workers, right from the start of research, in international scientific meetings. The direct contact with specialists in their field is of primary importance for stimulating the interest and future activity of research workers.

Sometimes colloquia and discussions are more valuable than a long period of library work. Exchange of ideas is of major importance and encourages international scientific collaboration.

The regular international conferences consist of plenary and keynote lectures, intended to give an authoritative or provocative survey (they do not always succeed!), and communications of research results either as brief lectures or as 'posters'. The posters present the material in brief but readily legible form and allow extended and free discussion between the authors and any participants interested in the subject.

In our opinion this scheme gives the broadest scope for direct exchange of scientific information, especially when it is supplemented by adequate time for personal meetings and discussion. At the same time it must be admitted that many such meetings are far too large, the need for parallel sessions limiting the choice of lectures to be attended by any one person, and personal contact being sometimes very difficult or even impossible to arrange.

## CHAPTER 2

# Teaching Analytical Chemistry

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### 2.1 INFORMATION

#### 2.1.1 General Information

"The electric current could never possess such power as the electricity contained in the printed word" [57]

In any domain of human activity, to be informed is now a prime necessity. Information is not only a social requirement but also a psychological necessity. To communicate with other human beings, an individual can develop psychically only if he continuously develops his knowledge and accumulation of information.

The multitude of human activities and the whole of civilization are based on transfer of information, which represents for man the most reliable way to achieve mutual understanding and present projects and to ensure future progress.

Scientific information is that obtained during scientific research. It ensures for science a connection between research and material production, and between science and other human activities.

The appearance and evolution of scientific information are consequences of the development of science. There is a feed-back to science from the information it produces, so scientific information is in a sense self-generating, and because it is largely uncontrolled proliferates rapidly; hence the literature or information 'explosion'. It is a branching chain reaction.

The era of the individual investigators is almost over. Current scientific progress is generally regarded as strongly dependent on documentation of the existing data and accumulated knowledge in a given science field and the application of information science to its organization and retrieval.

The amount of accumulated scientific knowledge has increased tremendously within the last few decades, the interaction of man and science falling into three main periods, as follows [58].

In the Renaissance, a scientist could know practically all human knowledge in almost all domains. As an example, Pico de la Mirandola claimed to know the 'whole' science.

At the beginning of the present century, a physicist, chemist or naturalist knew virtually all the scientific results in his field. The French chemist Marcelin Berthelot said on his death-bed: "You are present at the death of the last man who knew the whole of chemistry".

Today, at the start of the ninth decade of our century no scientist can have read all the papers in his own research field, and the number of scientific or technical disciplines is continuously growing. The age of specialization has arrived.

Any research work must begin with a literature survey. To neglect it is to risk 'rediscovering' facts already known, or what is worse, to find erroneous solutions to research problems already solved. In exchange, when the work is complete the results should be made accessible to other people; otherwise the work is not a true contribution to progress.

The earliest significant step in the spreading of information was Gutenberg's invention of printing. Over five centuries elapsed before the appearance of the present 'Gutenberg Galaxy', the overwhelming amount of printed information.

From colloquial discussions between groups of scientists or correspondence between colleagues having similar scientific interests, the first scientific societies were created in Italy, England and France in the second half of the 17th century, and these gave rise to the first periodical publications, such as *Accademia del Cimento* in 1657, or *Philosophical Transactions* and *Le Journal des Scavants* in 1665 [59]. The number of scientific journals thereafter rapidly increased, as the volume of knowledge increased:  $10^2$  journal titles were recorded in 1800;  $10^3$  in 1850;  $10^4$  in 1900 and  $10^5$  in 1960. If this rate of growth is maintained, at the end of this century there will be about a million titles.

These data fit the exponential expression:

$$x = 2^{(t-t_0)/m}$$

where  $x$  is the number of journal titles at time  $t$ ,  $m$  the time interval in which the number of journals is doubled, and  $t_0$  is the date of the first journal. If  $m$  is taken as 17-18 years, and  $t_0$  as 1680, we get the following results:

$$x_{1800} = 2^{120/18} \sim 100; \quad x_{1900} = 2^{220/17} \sim 10,000;$$

$$x_{1850} = 2^{170/18} \sim 1000, \quad x_{1960} = 2^{280/17} \sim 100,000$$

which agree with UNESCO statistics [60].

The famous library of Alexandria founded by Ptolemy I, King of Egypt, about 300 B.C., contained over 600,000 parchments (equivalent to about 100,000 books of today) [61]. By comparison, contemporary libraries are immense. The American 'Harvard' library has over seven million volumes, the library of Moscow State University receives a million volumes yearly.

The parallel in development of science and its literature is graphically brought home by the fact that 90% of all scientists since the world began are alive and working today.

The number of research workers doubles in ten years, so of course there is a corresponding increase in the number of scientific publications. However, the number of *fundamental* discoveries takes about 45 years to double.

The scientist at present is faced with an annual production of approximately 2,000,000 articles, 75,000–120,000 books, 300,000 patents and inventions, and an unknown but large number of unpublished scientific reports [59].

Because of the increase in the number of scientists and their productivity, and other factors such as new reproduction techniques (photocopies etc.) the amount of information circulated in the developed countries in 1985 will be about five times that in 1970 [62].

If to this enormous scientific production we add the knowledge accumulated in the past, it is obviously practically impossible for a specialist to know all the papers related to his scientific interests. The quality of his scientific creativity is to some extent conditioned by this fact.

Unfortunately for science, a great deal of the contemporary information arises from redundant papers or papers of low scientific value and content. Boutry [63] says much the same: "the variation and the volume of publications are generally independent of their content, ... or almost 80% from scientific papers could as well never be published ... or the volume of papers of the paid research workers taken in their totality, risks not to be determined by what they wish to communicate as new or useful, but by the fact that they must publish something at regular intervals of time".

Brown [64] draws similar conclusions: "There can be no doubt in the mind of anyone dealing with scientific literature that much need never be produced and of that which justifies its appearance, 80 per cent could be improved by drastic reduction in length and by clear writing".

Many scientists consider that restrictions should be imposed, in the first place by the authors themselves, so that a given piece of work is published only once, and not several times under various disguises. Far too many articles are redundant in content. According to UNESCO statistics, of every 100 published papers, only 5 are useful for the development of science.

The same thing has happened with scientific books. Moravia [65] says: "... the first condition for a book to be truly 'read' is that that book be truly 'written'. ... The book will be saved if books will be 'written', otherwise it will perish if we shall limit ourselves only to 'print' them".

The sheer volume of information available produces the risk that man will be transformed from the master to the slave of information, from a critical filter to a supersaturated storehouse of information, from a brilliant creative mind to a mechanical collector of truth.

The confrontation between scientists and the results of their own activity

sometimes leads to problems, caused by various factors such as the amount of informational material, language difficulties, different types of information transfer, etc.

The fear of inflation of documentation is very old. Barnaby Rich (1613) asserted: "One of the diseases of this century is the multitude of books; the world is overwhelmed by them, it cannot digest the plenty of useless printed material which is daily produced and widespread in the world" [66].

One of the effects of the vast increase in information is that the *concentration* of valuable material is continuously decreasing because of the growing dilution with useless facts. Further just as happens with other natural resources it becomes correspondingly more difficult to separate the useful from the useless as the richness of the deposits decreases.

A judicious selection of technical and scientific information should be imposed [67] before it is too late for it to be achievable.

It has been estimated that 95% of the truly 'original' scientific papers come from only 5% of the working population of scientists, but these papers might never be published but for the work of the other 95% of scientists who have not themselves made important contributions to the development of science. This assertion is supported, for example, by the case of insulin. In 1904, the French physiologist Grey observed that intravenous injections of pancreas extract reduce the glucose content of animals which have had their pancreas removed. The same observations were subsequently made by Minkowski and von Mering, but they did not see the implications for treatment of diabetes. In 1921, the Romanian physiologist Paulescu published the results of his research on the isolation of the hormone pancreatine (insulin), which had a hyperglycaemic effect. In 1922, Bauding culminated his own researches by using pancreatine extract for the cure of diabetes.

The development of scientific knowledge has resulted in diversification of informational resources, into (a) direct communication (scientific meetings, lectures, etc.), (b) documents and (c) access material (catalogues, index cards, computerized storage and retrieval etc.).

The most important documentation sources may be subdivided into:

- (1) primary sources (periodicals, reports, patents),
- (2) secondary sources (abstracting journals, lists of titles of conference and journal papers),
- (3) tertiary (special) sources and services (bibliography of bibliographies).

The research worker may spend up to 30-35% of his working time on documentation, to the detriment of his laboratory activity. This is one reason why he may resort to use of well-organized documentation services.

In the past, information was transmitted by rather rudimentary means. The modern method is by 'transplantation'. For this the information must have a support: paper on which information is printed, punched cards, punched tape.

magnetic tape, etc. This method of information transmission presents the advantage of low noise but has the disadvantage of low transmission rate.

Another 'support' for information transmission is provided by electric or electromagnetic signals. The transmission rate is thereby considerably increased, but the information may be disturbed during transmission.

The accumulation of a large number of scientific data in different domains necessitates their statistical processing, which in essence is a synthesis of collected and processed data. Electronic computers facilitate the operations of statistical processing.

The development of informational transfer necessitated a corresponding development of means of collecting, transmitting, processing and storing information. The discovery of writing, the invention of printing and transmitting devices all contributed to the use of information.

The abacus may be considered the first device for information processing. Then in the 17th century Blaise Pascal invented the first arithmetic machine with toothed wheels. Mechanical or electromechanical arithmetic machines were later invented by Babbage, Turing and others.

At the end of the fifth decade of this century, the first electronic computer, valve-operated, was constructed at Harvard University. In the following 30 years, the second (transistor and semiconductor) and third (integrated circuit) generations of computers appeared, closely followed by the fourth and latest generation, characterized by the use of high-density generalized integrated circuits and MOS (metal oxide on silicon) type memories.

Many feel that we can now answer 'yes' to the question "Can mankind solve the problem of the informational explosion?", this optimism being based on the one hand on the potential capabilities of the human brain and on the other on the development of the necessary technical means, namely the electronic computers. They point to the use of electronic computers for the organization of subject and author indexes [68], as an example. At present, over 70 journals use computers for this purpose, sometimes with unhappy results. Other journals are experimenting with synoptic publication coupled with microfiche or microfilm storage of the full text, and other means of rapid documentation and selective transmission of information.

The progress achieved so far by informatics (the science of automatic processing of information) has led to the prediction that by 1995 all information will be stored only centrally and made universally available to users.

Others take a more pessimistic view, on the grounds that computers do not exercise value judgements, so storage and retrieval systems will give as much dross in the output as was in the input. In other words a new science of analytical informatics is needed to perform the operations of analytical chemistry (separation, concentration, evaluation) on the raw material (information) of science. Without such a preliminary sifting, the information given to the unfortunate user of the informational services will require him still to sacrifice laboratory time! We shall consider this further in the next section.

### 2.1.2 Information in Chemistry

Like other disciplines, chemistry uses all the ways of transmitting information: direct communications, documents and services.

Direct contacts between specialists, which are an important means of transfer of knowledge, have become aleatory owing to the large number of scientists working on a given problem or related research problems. Moreover, international participation in the scientific meetings, conferences or congresses organized in different countries is somewhat limited for geographical or economic reasons.

Laitinen [69] comments "Whatever the details of procedure, most of our scientific meetings would benefit from increased participation by our colleagues from overseas. Communication of current progress by personal contact represents a largely intangible but nevertheless important stimulus in creative work, and its effectiveness should not be severely limited by geographical barriers".

The direct study of documents has the advantage that research workers can form their own appreciation of the utility of the information, make unforeseen associations of ideas, and formulate new hypotheses.

From the immense array of primary documents (scientific and technical reports, communications, papers, monographs, handbooks, etc.), chemists consult periodical journals in particular.

The first chemical journals appeared in the 18th century, such as the *Chemisches Journal* (1778–1784), *Chemische Annalen* (1784–1803), *Annales de Chemie* (1789), and later the *Annalen der Pharmacie* (1832), which became Liebig's *Annalen der Chemie* in 1848. The number of chemistry journals today is enormous but only about 200 are ranked high in importance [70].

As the number of journals has increased, so has the number of languages in which they are written. This makes it more difficult for the research worker to survey the original literature. It has been estimated that if a chemist who knew 30 languages read for 40 hours every week at the rate of 4 papers per hour, he could read in a year only 5% of the primary source papers now published. It is because of this avalanche of information that the ordinary chemist turns to the secondary sources of information, obtained by selective processing of the primary material, their purpose being to give in concise form the essence of the original information and to state its primary source.

The secondary sources include abstracts, bibliographies, catalogues, contents journals, computerized indexes [subject, author, title or bibliographic reference, patent number, compound name or reference number, alphabetic (CZU), keyword in context (KWIC) or out of context (KWOC), reports], meeting abstracts, reports, reviews, etc.

Chemists prefer mainly abstracts, reviews and reports. These forms of documentation are quite old, initiated by individual journals and by chemical societies, and giving in condensed form the content of recently published papers. They may be said to have been originated by Berzelius in his annual *Jahresberichte*, which began in 1821 and reviewed all chemical and mineralogical publications

that had appeared during the year. Perhaps the first periodical journal to give abstracts was the fortnightly *Chemical Gazette*, established in 1843, and succeeded in 1860 by the weekly *Chemical News*. These were commercial journals and gave very rapid publication indeed. The issue of *Chemical Gazette* for 1 May 1847 carried a translation of a paper given in Paris on 29 March 1847. The French Chemical Society published abstracts in its *Bulletin*, from 1858 to 1947 (in alternate volumes). The German Chemical Society published abstracts in *Berichte der Deutschen Chemischen Gesellschaft* from 1868 to 1896, and then in 1897 took over *Chemisches Zentralblatt* (which began life in 1830 as *Pharmaceutisches Central-Blatt*). *Zeitschrift fur analytische Chemie* (1862) published abstracts of analytical papers from the beginning, and *The Analyst* (1876) seems to have begun doing so in about 1883. The American Chemical Society published general chemical abstracts in its *Journal* from 1897 to 1906, and established *Chemical Abstracts* in 1907. The Society for Analytical Chemistry founded *Analytical Abstracts* in 1954, as a successor to the *British Chemical Abstracts Section C*, which ceased publication in 1953.

An important role in the classification and storage of chemical information is played by notation and indexation.

In an article entitled 'Milestones in Chemical Information Science', Skolnik [61] briefly presents the evolution of indexation, beginning with Richter's use of empirical formulae for tables of compounds (1884), the contribution of Luhn (1958–1959), the KWIC system, and processing on the IBM 704, and ending with the best results obtained in this domain up to 1975. He also shows the need to find new computerized chemical information systems capable of helping chemists to correlate chemical structures with properties.

Such a wish may be achieved in the near future, as Elgozy [71] asserts: "The new world of informatics is too recent a discovery for the pioneers to have time to search all their territories, to clear the jungle and to prospect all their resources".

The broadest generalization of information is found in reference works such as treatises, encyclopaedias, etc. The first significant encyclopaedia of chemistry was the *Dictionnaire de la Chimie* in 4 volumes by Mocquer (1778), and the first important treatises appeared in the 19th century: Gmelin's *Handbuch der anorganischen Chemie* (1817) and Beilstein's *Handbuch der organischen Chemie* (1881). This kind of tertiary source has been extensively developed in the course of time.

In parallel with the increase in volume of scientific and technical information, information services have been organized in national or international institutes, capable of furnishing bibliographic data, or selected scientific and technical literature, survey reports, etc.

Even so, a few research workers still prefer to consult only a limited number of primary documents in the library, ignoring the secondary or tertiary sources or the information services, partly perhaps from fear or ignorance of the technical

services available, and partly from mistrust of relying on others (although in fact they are doing so when they use the primary literature).

It is interesting to try to assess the efficiency of the various ways of gaining information. For example, a study based on a questionnaire [72] on how the literature should be studied in American colleges and universities, showed that the means of information most used were *Chemical Abstracts* and *Beilstein*, and to a less extent *Science Citation Index*.

Wubbels [73], at Grinnell University (Iowa), teaches students to study the chemical literature, in the framework of his organic chemistry lectures. He says: "The benefits include possibilities of closer relationships of advanced courses to original literature, and better student preparation for independent projects or research efforts".

To estimate the informational efficiency of the chemistry journals, Pinski [74] defines three measurements of influence: influence per weight (based on ratio of references *to* and references *by* the journal), influence per publication and total influence. He used for this study 200 chemistry journals cited in *Science Citation Index* (SCI) and an electronic computer to process the data relating references and quotations from other journals, and length and number of the articles. The results of such a study are given in Table 2.1. The values of the three 'influences' increase with the informational efficiency.

Table 2.1

Influence measures and publication data for subfields of chemistry [70]

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Copyright by the American Chemical Society)

Subfield	Infl. wt.	Refs./pub.	Infl./pub.	Pubs.	Tot. infl.
GEN CHEM	1.043	15.72	16.40	16089	263809
BIOCHEM	0.747	20.65	15.42	12049	185749
ANAL CHEM	0.737	11.78	8.69	4243	36860
ORGAN CHEM	0.598	14.24	8.52	5968	50855
INORG CHEM	0.776	14.47	11.23	2515	28244
APPL CHEM	0.846	12.22	10.34	2762	28571
POLYMERS	0.567	11.37	6.39	3224	20614
PHYS CHEM	1.340	12.37	16.58	7188	119206
CHEM PHYS	3.218	15.71	50.54	3220	162732

### 2.1.3 Information in Analytical Chemistry

There are two streams of analytical information: the literature and the laboratory experimental work. The two are interdependent in the sense that the experimental results enrich the literature, which in turn is used to guide, orient and develop practical activity in the laboratory.

As in other scientific disciplines, the output of information in analytical chemistry increases yearly. The annual amount of information from all analytical chemistry journals is estimated as being  $10^9$  bits [74], so the analyst is confronted with a miniaturized version of the overall information problem, and must use all the techniques available for dealing with it. By his very nature, he will want to try to analyse the information itself. For example, the statistical processing of the analytical chemistry journals over given time intervals is particularly useful for drawing conclusions about trends in development.

First, the development of analytical chemistry can be compared with that of chemistry as a whole. Brooks and Smythe [75] have examined this for the period 1910–1970 and conclude that except for small fluctuations, the rates of development are similar.

From another study [76] dealing with the years 1965, 1970 and 1975, there appears to be a small decrease in analytical chemistry publications relative to the chemical publications in general (Table 2.2).

**Table 2.2**  
Number of publications on analytical chemistry.

Values in parenthesis are based on the assumption that only half of the papers on analytical chemistry are abstracted in Analytical Abstracts [76] (by permission of the copyright holders, Elsevier Publishing Co., Amsterdam).

Subject	1965		1970		1975	
	Number	%	Number	%	Number	%
Chemistry	180,000	100	276,600	100	332,300	100
Analytical chemistry	6640	3.7 (7.4)	9820	3.6 (7.2)	8980	2.7 (5.4)

The number of analytical chemistry books has increased arithmetically [75] as shown in Fig. 2.1, but discontinuously, the influence of the two world wars being obvious. There has been a significant increase in the number of journals of analytical chemistry, however, as shown in Fig. 2.2, though even the much sharper increase after the end of the last world war is arithmetic rather than geometric.

It is perhaps most significant of all that over 30% of papers published on analytical chemistry appear in a total of only 13 journals.

These major journals, each containing at least 1% of all articles published, are, in alphabetical order: *Analytica Chimica Acta*, *Analytical Biochemistry*,

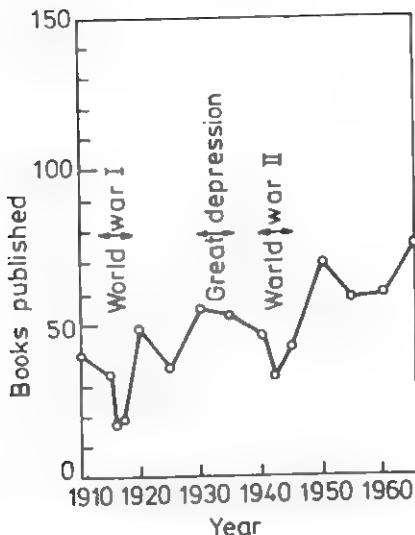


Fig. 2.1 Number of books on analytical chemistry published in the period 1910-1966 [75] (by permission of the copyright holders, Pergamon Press, Oxford).

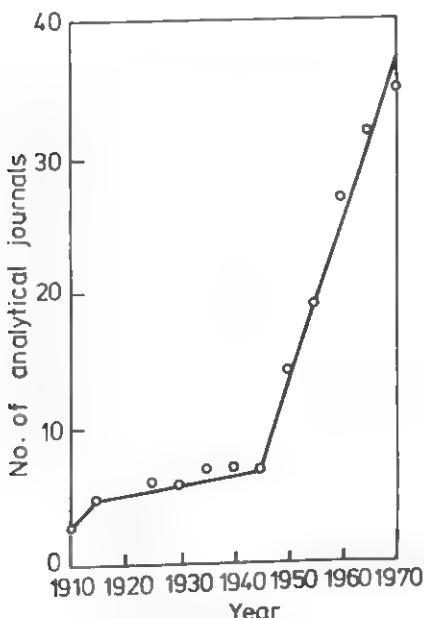


Fig. 2.2 - Cumulative total of journals catering exclusively (or almost exclusively) for analytical chemistry [75] (by permission of the copyright holders, Pergamon Press, Oxford).

*Analytical Chemistry*, *Japan Analyst (Bunseki Kagaku)*, *Journal of Electroanalytical Chemistry*, *Journal of the Association of Official Analytical Chemists*, *Mikrochimica Acta*, *Nukleonika*, *Talanta*, *The Analyst*, *Zavodskaya Laboratorya*, *Zeitschrift für Analytische Chemie* and *Zhurnal po Analiticheskoi Khimii*.

From a questionnaire addressed to the authors of articles published in *Analytical Chemistry* [77], it appears that those replying considered the most important journals to be (in descending order) *Anal. Chem.*, *J. Am. Chem. Soc.*, *J. Chromatog.*, *Anal. Chim. Acta* and *Environ. Sci. Technol.*, but of course this may be construed as reflecting the kind of work covered by the papers in *Anal. Chem.* as much as the interests of those (87%) interested enough to reply.

Influence measures [70] show that generally the most important analytical chemistry journals are *Anal. Chem.* and *J. Chromatog.* (Table 2.3), in agreement with the questionnaire results, though it may be suggested by some that national or sectional interests contribute to the influence results.

Table 2.3

Journal assignments and influence measures (1973 data) Analytical chemistry [70]  
(Extracted with permission from *J. Chem. Inf. Comput. Sci.*, 1977, 17, 67.)

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Journal	Infl./wt.	Refs./pub.	Infl./pub.	Pubs.	Tot. infl.
ANAL LETTER	0.40	7.2	2.9	123	353
ANALUSIS	0.12	8.5	1.1	85	90
ANALYST	0.82	9.7	7.9	131	1039
ANALYT CHEM	0.75	20.9	15.6	603	9401
ANALYT CHIM	0.51	8.9	4.5	344	1555
J AOAC	1.04	5.1	5.3	321	1692
J CHROM SCI	0.94	11.9	11.2	118	1317
J CHROMAT	0.53	10.7	5.6	631	3553
J RAD CHEM	0.20	6.4	1.3	143	186
J THERM ANA	0.34	9.7	3.3	45	147
JAP ANALYST	0.02	25.9	0.5	231	119
MICROCHEM J	0.31	7.5	2.3	86	201
MICROCH ACT	0.43	9.9	4.2	124	525
TALANTA	0.49	10.1	4.9	155*	763
Z ANAL CHEM	0.76	6.4	4.9	249	1210
ZH ANAL KH	0.15	8.4	1.3	463	602

\*We think this figure should be 194, and the average number of references per publication 16.7, so influence per publication should be 8.0 and the total influence 1587. We have not checked the other figures given.

The development of analytical chemistry in different countries can be related to the number of articles originating in these countries and published in journals of widespread circulation, and to some extent to the language they are written in. The contribution of various countries to the development of analytical chemistry is presented in Table 2.4, which shows that seven countries have made the greatest contribution in roughly the order: U.S.A. > Germany > U.S.S.R. > U.K. > France, Japan, Czechoslovakia. Four of these countries contributed 90% of the total of analytical papers published in 1910, but only 32.3% of that published in 1970. The U.S.S.R. and Japan accounted for only 2% of the 1910 total but in 1970 their contribution had risen to 36.1%. Seven countries which in 1910 published nothing were contributing approximately 17% of the total in 1970.

Authors tend to be nationalistic in choosing a journal to publish in. In 1976, for example, 46% of the articles published in *The Analyst* came from the U.K., 8.8% from India, 8.3% from the U.S.A., 5.2% from Canada, 5.3% from Australia, etc. [78]. Again, most papers published in *Analytical Chemistry* are American in origin, but the number of foreign papers doubled between 1969 and 1977 [77], mainly coming from Japanese (7%), U.K. (5%), Australian (5%) and Netherlands (4%) authors [79]. The papers published in *Analytical Chemistry* come from the following types of laboratory: academic 62.3%, industrial 18.6%, governmental 12.3%, others 6.8% [79].

Finally, the number of languages in which analytical papers are published has increased. In 1910 the articles were predominantly written in English (50.6%), German (32.9%) and French (12.4%). In 1970 the importance of these languages had obviously diminished, the figures being English (30.3%), German (8.1%), French (3.6%), and other languages had increased in importance: Russian (28.4%), Japanese (7.7%), Czech (5.6%), Spanish (2.6%), etc. [75].

The trend of development or regression in research on the analytical methods used within the period 1950-1970 is presented in Fig. 2.3. We stress 'research' in this context, because it is virtually impossible to arrive at a realistic appraisal of the extent of *use* of the methods; it is interesting, however, that an attempt at such a survey elicited the information that titration is the most frequently used method.

Figure 2.3 shows that research in methods such as organic polarography, atomic absorption, atomic fluorescence, N.M.R. and nucleonics has obviously tended to increase markedly. Raman spectroscopy has undergone a resurgence since 1956. Classical techniques (gravimetric and titrimetric) remain remarkably constant in popularity as research topics, which is interesting in view of the continuous propaganda in support of instrumental methods. Separation methods also remain popular, except the distillation techniques, which are in decline.

The general trend of development of analytical methods has been examined by Fresenius [80]. Like other techniques, analytical methods have an evolutionary period, followed by expansion and consolidation, and then become static or go

**Table 2.4**  
Percentage of analytical work carried out in various countries [75] (by permission of the copyright holders, Pergamon Press, Oxford)

Country	1910	1915	1920	1925	1930	1935	1940	1945	1950	1955	1960	1965	1970
	Year												
U.S.S.R.	1.0			0.8	5.7	29.4	30.8	18.2	17.8	13.0	22.9	25.4	28.4
U.S.A.	28.9	30.4	25.3	13.4	18.8	14.6	25.0	48.3	19.9	18.0	20.7	15.8	17.7
Japan	1.0	1.0		3.2	2.6	3.1	2.9		5.0	12.3	7.7	11.0	7.7
Germany*	31.9	30.4	19.9	39.7	26.3	16.4	10.5	2.5	6.7	12.1	4.8	6.4	6.1
U.K.	17.6	20.2	12.3	11.9	10.5	6.4	7.1	12.4	12.0	8.2	6.0	4.3	5.9
Czechoslovakia	-			4.8	3.5	2.8	1.7		6.0	8.1	3.8	5.3	5.6
France	10.3	4.5	21.0	7.1	14.5	7.6	3.8	2.5	9.2	4.7	3.1	3.5	2.6
India					1.3	1.8	0.8	2.1	0.6	4.3	5.0	3.5	2.6
Scandinavia	1.1	1.8		3.9	1.8	0.8	2.1	2.6	3.3	2.4	1.0	0.7	2.1
Romania	2.3	3.5		4.8	0.8	0.4			0.8	2.0	3.5	2.0	
Poland					2.2	2.0	—			1.6	1.5	4.1	1.8
Spain	2.1	1.1	1.8	0.8	2.2	2.1	2.5	1.6	4.2	1.8	1.7	1.8	1.5
Netherlands	3.4	8.8		3.2	1.3	1.5	2.9	0.5	0.8	0.8	0.8	0.8	1.3
Italy	1.1		4.0	1.8	4.1	2.5			2.3	4.2	2.5	1.7	1.0
China					2.6	—		0.8		5.6	3.1	—	
Rest of the World	7.2	4.4	5.1	2.4	7.7	4.0	7.0	9.3	11.4	7.7	10.9	9.1	11.1

\* Includes both East and West Germany.

into decline. It is interesting to see how this applies to currently popular analytical methods.

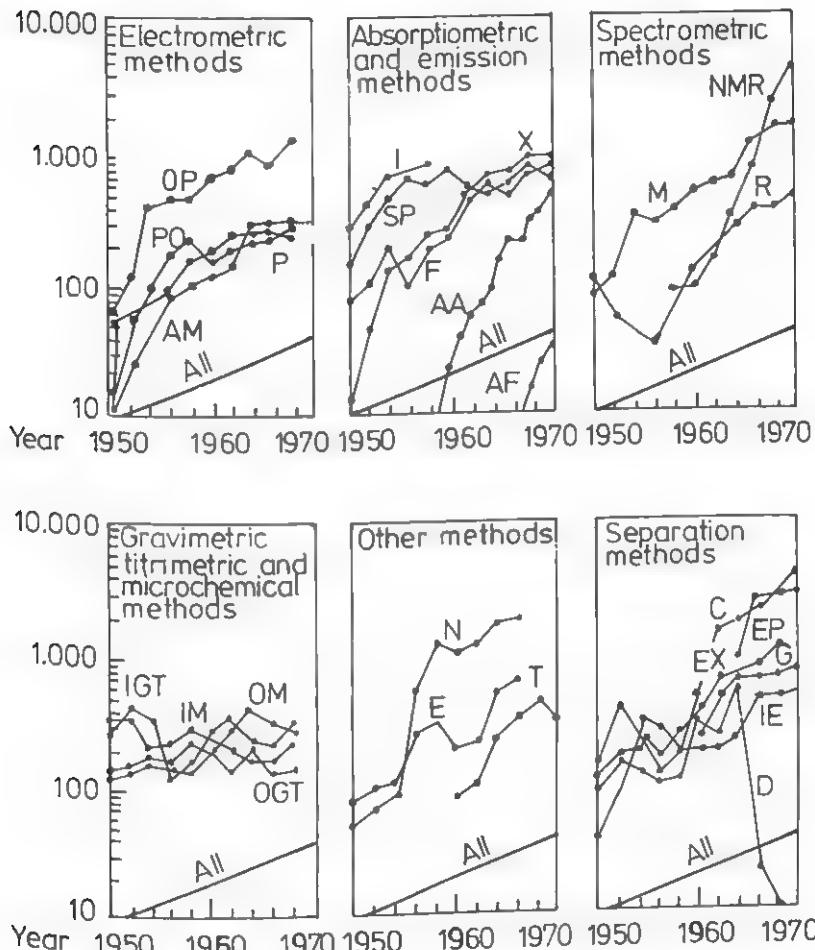


Fig. 2.3 Methods used in analytical chemistry during the period 1950–1970. Data expressed as percentage of total numbers of papers. AM, amperometry; OP, organic polarography; P, polarography; PO, potentiometry; AA, atomic absorption; AI, atomic fluorescence; F, fluorimetry; I, infrared spectroscopy; SP, spectrophotometry; X, X-ray fluorescence; R, Raman spectrometry; M, mass spectrometry; NMR, nuclear magnetic resonance; IGT, inorganic gravimetry and titrimetry; IM, inorganic microchemistry; OGT, organic gravimetry and titrimetry; OM, organic microchemistry; E, electron microscopy; N, nucleonics; T, thermal analysis; C, chromatography; D, distillation; EP, electrophoresis; EX, extraction; G, gas-chromatography; IE, ion-exchange [75] (by permission of the copyright holders, Pergamon Press, Oxford).

Brooks and Smythe [81] have made a detailed study of the development of atomic-absorption spectrometry. They show (Fig. 2.4) that between 1955 and 1970 the development of this technique can be described by a sigmoidal (logarithmic) curve. In comparison with 25 articles on atomic-absorption written in 1960, which represented 0.25% of the total number of articles on analytical chemistry, in 1970 there were 662 articles, or 3.4%. Figure 2.4 also shows that the proportion of papers on atomic-absorption spectrometry in the literature stabilizes at 4% in the first six months of 1970. The articles on atomic-absorption spectroscopy are about equally divided between those dealing with the equipment and those on application [81], as shown in Table 2.5.

Braun, Lyon and Bujdosó [82] have similarly examined the literature of activation analysis. They conclude that over the last 35 years the number of published articles has doubled every 3 years, as shown in Fig. 2.5, but the growth-rate of publications on 14-MeV neutron generators has decreased in

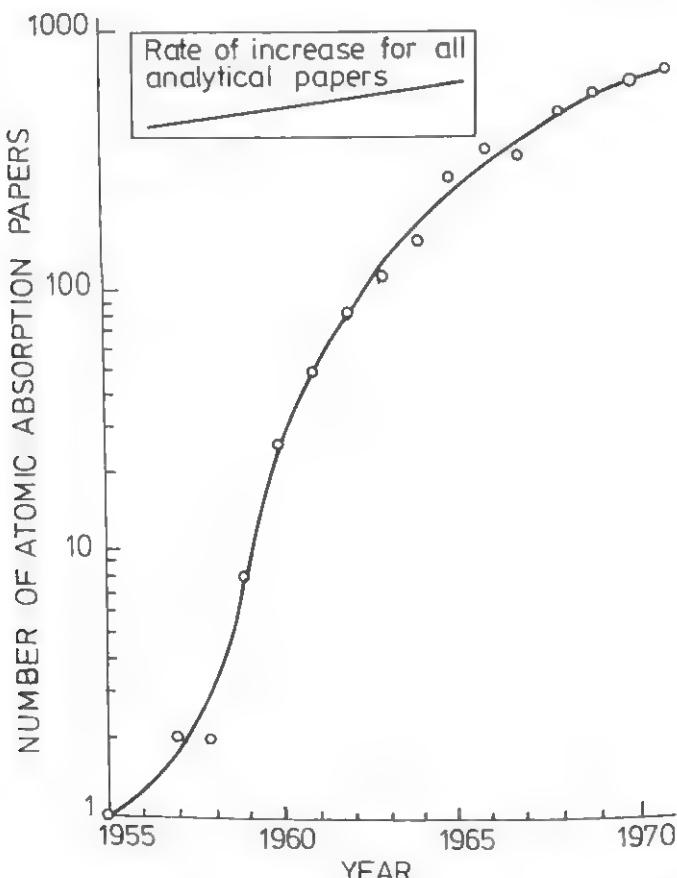


Fig. 2.4 Annual publication rate of atomic absorption papers [81] (by permission of the copyright holders, Elsevier Publishing Co., Amsterdam).

Table 2.5

Percentage of atomic absorption papers in various general categories [81]  
(by permission of the copyright holders, Elsevier Publishing Co., Amsterdam)

Category	Year					
	1961	1963	1965	1967	1969	1971
Agricultural	3.6	1.8	3.3	4.9	4.9	5.4
Biological	17.9	10.9	19.8	17.9	17.9	12.9
Food	—	—	1.1	4.6	2.0	3.2
Geochemical	3.6	3.6	10.9	9.8	10.4	10.2
Industrial	3.6	5.5	9.9	8.4	9.3	9.7
Instrumental	25.1	49.1	39.6	44.2	44.6	47.9
Metallurgical	14.2	20.0	7.7	7.7	9.2	9.8
Reviews	32.0	9.1	7.7	2.5	1.7	0.9

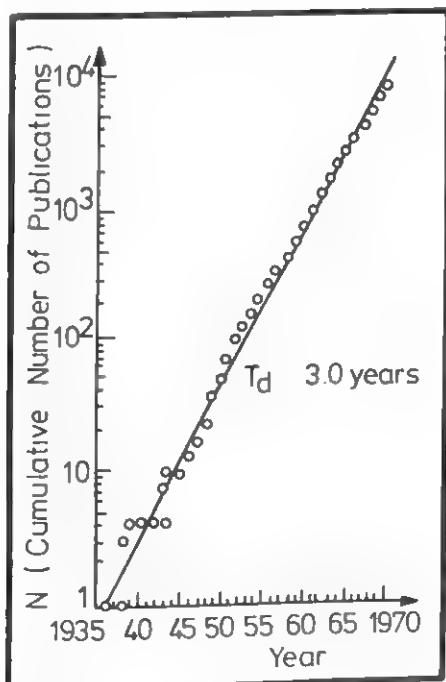


Fig. 2.5 Growth of publication on activation analysis [82]. (Reprinted with permission from *Anal. Chem.*, 1977, 49, 682A. Copyright by the American Chemical Society.)

the period 1959–1973 (Fig. 2.6). The same authors have established ‘ages’ for the development of neutron generators, as shown in Fig. 2.7.

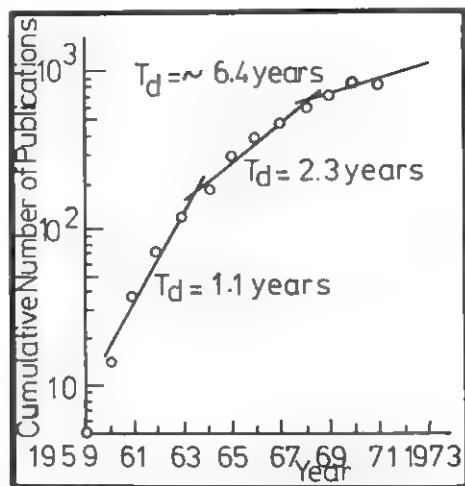


Fig. 2.6 Growth of publication on activation analysis by 14-MeV neutron generators [82]. (Reprinted with permission from *Anal. Chem.*, 1977, 49, 682A. Copyright by the American Chemical Society.)

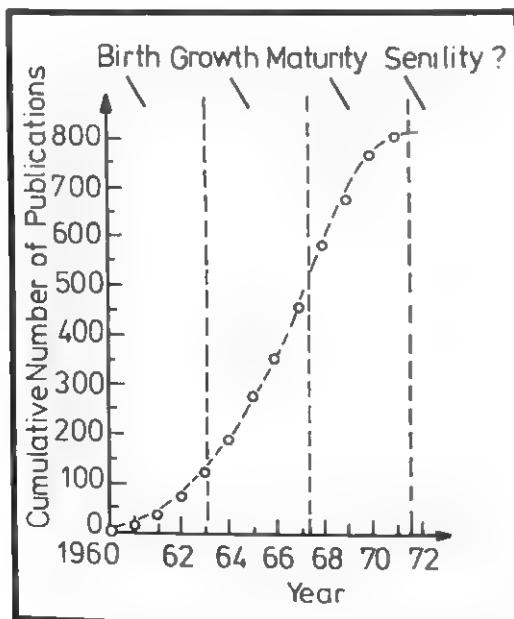


Fig. 2.7 – Four ages of neutron generators [82]. (Reprinted with permission from *Anal. Chem.*, 1977, 49, 682A. Copyright by the American Chemical Society.)

Another technique frequently used in analytical chemistry is chromatography. Berezkin and Chernysheva [76] have examined the trends in its development. In terms of published papers chromatography shares first place with spectrometry among analytical methods (Table 2.6). It is particularly useful in the analysis of organic compounds and gases, as seen from Table 2.7.

As with techniques in general, the individual types of chromatographic methods wax and wane in popularity as fashions come and go (Table 2.8).

**Table 2.6**

Percentage of publications on separate branches of analytical chemistry [76]  
(by permission of the copyright holders, Elsevier Publishing Co., Amsterdam)

Method	1965	1970	1975
Chromatographic	24	30	27
Gas chromatographic	8	11	9
Spectroscopic (EPR, NMR, photometry)	36	37	36
Electrochemical	10	13	20
Gravimetric, titrimetric, etc.	30	20	17

**Table 2.7**

Percentage of publications on different branches of the analytical chemistry of organic compounds and gases [76] (by permission of the copyright holders, Elsevier Publishing Co., Amsterdam)

Method	1965	1970	1975
Chromatographic	39	48	44
Gas chromatographic	14	17	15
Spectroscopic (EPR, NMR, photometry)	29	29	31
Electrochemical	17	16	18
Gravimetric, titrimetric, etc.	15	8	7

**Table 2.8**

Distribution of publications according to type of chromatography [76]  
(by permission of the copyright holders, Elsevier Publishing Co., Amsterdam)

Type	1970	1975-76 (first 6 months)
Gas chromatography (GC)	29	26
Paper chromatography (PC)	13	7
Thin-layer chromatography (TLC)	32	28
Column liquid chromatography (CLC)	26	39

Though such ‘informatics’ studies are interesting, and useful in indicating trends, the sceptic will wonder about the validity of some of the criteria used. Specialist journals tend to be inbred in terms of the citations in references, for example, and it is notoriously easy for authors to quote their own work to the exclusion of that of rivals. There also tend to be the nationalistic tendencies on the part of some authors, which may lead to an imbalance in the consultation of journals and hence in citations. The results are probably best treated as qualitative rather than quantitative.

In other applications, however, information theory may give more objective criteria of quality. For example, it has been used for choosing the best combination of chromatographic columns to use for identification purposes in gas chromatography [83, 84]. Further, while it is traditional to assess the performance of a new analytical method by statistical analysis of the results, an additional criterion is obtained by applying information theory to determine the informational power of the technique [85].

Because of the exponential increase in information, the accompanying increase in entropy is too large to be dealt with by the ordering capacity of the human mind without assistance, and that is why attention has been given to the use of computerized processing and retrieval methods, coupled with development of pattern recognition and machine identification methods [85, 86].

We conclude this section with Garfield’s observations [87]: “One can argue, that it is primarily the impact of the computer that has accelerated the transition of the laboratory chemist into the information chemist. Sociological and behavioral changes of this kind are not easy to measure. However, in addition to computer consciousness I believe the average working scientist today is far more information conscious than his counterpart 25 years ago”.

## 2.2 EXPERIMENTAL

“Experience is the interpreter of the wonders of nature. It never misleads us, only our grasp of it can do that. Until we can establish a general rule, we must accept the aid of experience. Though nature begins with the cause and then the effect, we must do the reverse and use experience to discover the cause.”  
Leonardo da Vinci

### 2.2.1 Reactions

In an article entitled “Chemicals: How many are there?”, Maugh [88] comments that “one measure of the answer is provided by the American Chemical Society’s Chemical Abstracts Service (CAS). As of November 1977 CAS’s unique computer registry of chemicals contained 4,039,907 distinct entities. The number of chemicals in the register, moreover, has been growing at average rate of about 6000 per week”. It is obvious that the number of known chemicals will continue to grow, probably at an increasing rate.

This multitude of chemicals forces analytical chemistry to develop new techniques for faster and highly reliable *identification* of substances, which is one of the main reasons for the rapid development of instrumental techniques and automation. This emphasis on the need for techniques for identification must be kept in perspective, however. For one thing, most of these chemicals have been made in the course of 'pure' research, and are unlikely to be met in practice other than as intermediates in the synthesis of other compounds or as the chemical equivalent of museum specimens of insects, plants, minerals, etc. The number of compounds actually *used* in industry or everyday life is comparatively small (though still a very large number), and the number of these that are likely to occur together in analytical samples in significant amounts (which may be at the trace level, of course) is smaller still, and is generally predictable from the history of the sample, the nature of the compounds, and their preparation or natural occurrence.

It follows that a prerequisite for identification is a sound knowledge of reaction chemistry, even when purely instrumental methods are used. Moreover, most instrumental methods have a resolving power sufficiently low for some preliminary chemical processes to be necessary, and if these are not properly understood and applied, the results may be erroneous. It is therefore imperative that chemists in general and analytical chemists in particular should receive thorough instruction in reaction chemistry; unfortunately this is often forgotten or ignored in modern chemistry courses. It is equally unfortunate that when reaction chemistry *is* taught, it is often done purely qualitatively, without regard to yield or special reaction conditions. Here lies the quintessential difference between analytical chemistry and organic or inorganic chemistry. The result is that students are often taught by means of *partially* true statements which are left unqualified, so that the student is left with the belief that they are *wholly* true. A typical example is the statement "manganese(III) is readily made from manganese(II) and permanganate"; it *is*, but *only* if there is a very large excess of the manganese(II), and even then in very low yield.

In the past, chemical reactions for analytical purposes were used mainly empirically. An important role in ordering this empirical material was played by the Swedish chemist Torbern Bergman. As Szabadváry remarks [89]: "Chemical analysis had been practised for two thousand years before Bergman, but it was he who gave it the status of a separate branch of science - Analytical Chemistry".

The study of chemical reactions and their mechanisms must always play an important part for the analyst, in both his training and research, since of necessity he must identify and use those reactions which will proceed quantitatively or completely reproducibly, and must know the conditions under which they will - or can be made to - do so.

The most important performance characteristics [90] of the reactions used for analytical purposes are sensitivity, selectivity and reproducibility. We can act

on these parameters only if we know thoroughly the 'chemism' of the reactions, in other words, have a sound fundamental knowledge of chemistry.

As Feigl [91] observed in the foreword of his book *Chemistry of Specific, Selective and Sensitive Reactions*: "Thus, studies and researches on the cause of specificity, selectivity and sensitivity of analytical procedures deserve attention for the following reasons: they extend the scientific basis of analytical chemistry; they furnish important points of reference and orientation in the research for new, analytically applicable reactions; and they initiate and stimulate work in many special fields of chemistry".

The study of reactions and the conditions under which they are used in analytical chemistry has been the subject of many books. We mention here those by Ringbom [92], Perrin [93] and Inczédy [94].

The study of chemical reactions is necessary for the future chemist to learn what chemistry is, in the same manner as learning about laboratory instruments shows him how to apply them. The use of properly chosen reactions in conjunction with an appropriate instrument gives perhaps an ideal connection of theory with practice.

For these reasons, modern teaching of analytical chemistry should contain a judicious mixture of reaction chemistry and instrumentation. Any large imbalance in the proportions may reduce the efficacy of the future research worker or specialist.

From the very structure of knowledge, it is obvious that the study of chemical reactions is self-propagating and practically unlimited. A new reaction introduced into analytical practice will be studied for many years and by many research workers, for optimization of operational parameters, study of the mechanism, structure of the products, etc. Whether these factors are of real importance or not, they will be seized on as raw material for the research factories.

We can illustrate this very well by considering the history of organic analytical reagents.

The use of organic reagents in analytical practice began in the 17th century. "Otto Tachenius, Pharmacist and Physician from Westphalia, describes in some detail (1666) the reactions of the aqueous extract of gall nuts with solutions of several metal salts, and thus may be credited with the publication of the first systematic examination of an organic reagent for metal ions" [95].

In the early stages, of course, the chemist (in his capacity as an analyst) had only a limited number of natural products available as organic reagents, and it was not until organic synthesis had been developed that a wide range of reagents was possible, and still later before systematic design and production could begin.

Table 2.9 shows some of the earliest synthetic organic reagents introduced into analytical practice, and still in use today in a variety of analytical techniques.

It is not sufficient, however, simply to know which chemical reactions may

be used in analytical chemistry. It is necessary to get maximum information from them.

Table 2.9

Organic reagents for metals (used for precipitation, extraction, absorptiometry or fluorimetry) [96] (by permission of the copyright holders, the Royal Society of Chemistry)

Reagent	Date
$\alpha$ -Nitroso- $\beta$ -naphthol	M. Ilinsky and G. von Knorre, 1884-85
Spot tests	F. Feigl, 1891†
Dimethylglyoxime	L. H. Tschugaeff, 1905
Cupferron	O. Baudische, 1909
8-Hydroxyquinoline	R. Berg, 1938*
2-Methyl-8-hydroxyquinoline	L. L. Merritt and J. K. Walker, 1944
Biquinolyl	J. Hoste, 1953
Morin	E. B. Sandell, 1940
Dithizone	H. Fischer, 1925

Authors' notes:

† This is Feigl's year of birth.

\* The date should be 1927; F. L. Hahn and K. Vieweg developed the use of the reagent independently of Berg.

Findeis *et al.* [97] give a good definition of the activity of an analytical chemist: "Today the analytical chemist is concerned about a wide spectrum of measurements. He is involved not only in determining what and how much is present (composition), but also what form (structure), how it is bound (valence), where it is spatially (location), and how uniformly it is distributed (homogeneity)".

It follows that analytical research and the teaching and application of analysis are now very complex, the teaching having the duty to show to the future specialist all these aspects of analytical science. An illustration is the study of the reaction of bivalent metal ions with *vic*-dioximes. After the introduction of dimethylglyoxime into analytical practice by Tschugaeff, the main interest was in its use for gravimetric determination of nickel. Owing to the high selectivity of this reaction, a series of research workers studied the possibility of obtaining new reagents of this kind for other metals, and of developing new working techniques using dimethylglyoxime. The selectivity of this reagent is mainly due to the low solubility of its complexes with nickel, palladium and platinum. Other studies on the complexes themselves, such as magnetic susceptibility measurements, have established that there is square-planar co-ordination geometry with two ligands per metal ion, co-ordinated through the ligand nitrogen atoms.

From pH measurements and the reaction with acetic anhydride, phenyl isocyanate, dimethyl sulphate and methylmagnesium iodide, it has been proved that one of the hydroxyl group protons on each ligand must be dissociated in order to give a neutral complex, and the other is rendered inert because of its involvement in hydrogen-bonding to the O<sup>-</sup> group resulting from the dissociation. Spectral studies of the compounds with *vic*-dioximes have led to their use in spectrophotometric methods. Structural studies by X-ray diffraction confirmed the data obtained with other methods and also revealed weak metal-metal bonding in the insoluble compounds. All these studies have been associated with use of the *vic*-dioximes in analytical practice. Tables 2.10 and 2.11 show some of the applications.

Table 2.10

Analytical applications of the *vic*-dioximes. Gravimetric methods [98]

(Reprinted with permission from *Anal. Chem.*, 1970, 42, No. 14, 56A. Copyright by the American Chemical Society.)

Nickel	Reagent(s)	References to Procedures
Nickel, macro	Heptoxime	Voter, Banks, 1949
	4-Methylnioxime	Banks, Hooker, 1956
	4-Isopropylnioxime	Banks, Hooker, 1956
Nickel, micro	Heptoxime	Ferguson <i>et al.</i> , 1951
	Nioxime	Voter <i>et al.</i> , 1948
Palladium	4-Methylnioxime	Banks, Hooker, 1956
	4-Isopropylnioxime	Banks, Hooker, 1956

Table 2.11

Analytical applications of the *vic*-dioximes. Extraction methods [98]

(Reprinted with permission from *Anal. Chem.*, 1970, 42, No. 14, 56A. Copyright by the American Chemical Society.)

Metal	Reagent(s)	Solvent	References to Procedures
Nickel	Heptoxime	CHCl <sub>3</sub>	Butts <i>et al.</i> , 1950; Gillis <i>et al.</i> , 1954
	4-Methylnioxime	CHCl <sub>3</sub>	Hooker, Banks, 1955
	4-Isopropylnioxime	CHCl <sub>3</sub>	Hooker, Banks, 1955
	4-Isopropylnioxime	Xylene	McDowell <i>et al.</i> , 1959
Palladium	Dimethylglyoxime	CHCl <sub>3</sub>	Nielsch, 1954
	4-Methylnioxime	CHCl <sub>3</sub>	Hooker, Banks, 1955; Banks, Smith, 1959
Rhenium	4-Isopropylnioxime	CHCl <sub>3</sub>	Hooker, Banks, 1955
	4-Methylnioxime	CHCl <sub>3</sub>	Kassner <i>et al.</i> , 1961

Another reaction noted for sensitivity and selectivity, and used for determination of  $\text{SO}_2$  in the atmosphere, is that proposed by West and Gaeke [99].

The reaction has three steps [100,101].

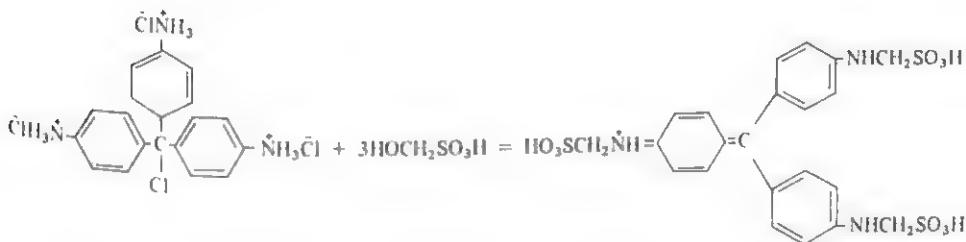
(a) complex formation:



(b) reaction between this complex and formaldehyde:



(c) reaction of the hydroxymethylsulphonic acid with pararosaniline hydrochloride:



The sensitivity of this reaction is very good, the detection limit being approximately  $10 \mu\text{g}/\text{m}^3$  [102]. To avoid interference from  $\text{NO}_2$ , *o*-toluidine [103] or sulphamic acid [104] can be added.

A disadvantage of the method is that the colour reaction is slow. Automation of the method [105] can overcome this disadvantage because the inherent reproducibility of the automated technique permits measurement to be made during the colour development instead of after its completion, but only at the expense of a corresponding decrease in sensitivity.

Other reagents have been tried in attempts to overcome this drawback of slowness of reaction, such as 4-(4'-aminophenylazo)-1-naphthylamine [106], which gives particularly high sensitivity, allowing determination of sulphur dioxide in solution at the  $0.07\text{--}2.4 \mu\text{g}/\text{ml}$  level. A 1:1 complex is formed.

Studies on the detection and determination of  $\text{SO}_2$  are still going on, because of its role as a pollutant. The pararosaniline method has undergone a series of improvements [107] as a result of optimization of the important parameters. Thus the pararosaniline is specially purified and standardized to reduce problems associated with its variability, and phosphoric acid is used to control the pH in the final colour development, liberate sulphur dioxide from the complex, and to complex heavy metals.

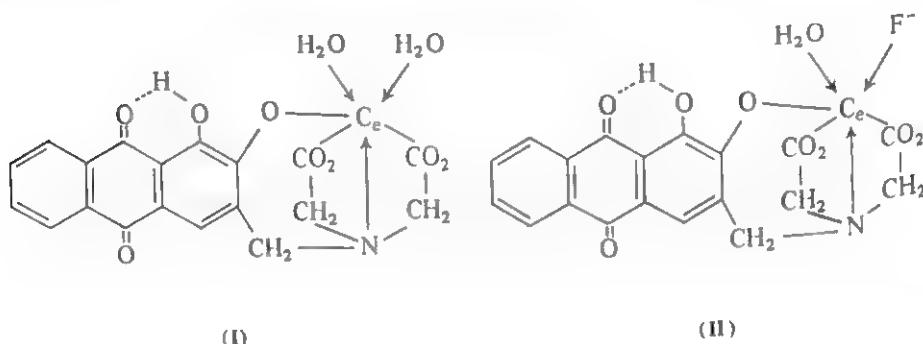
We have chosen this example to emphasize the importance of a systematic study on the conditions and the reaction mechanism.

Another reagent of particular analytical interest with regard to sensitivity and selectivity is [(3,4-dihydroxy-2-antraquinolyl)methyl]iminodiacetic acid (Alizarin Complexan or Alizarin Fluorine Blue), proposed by Belcher, Leonard and West [108].

This reagent was initially proposed as a complexometric indicator for the determination of Zn, Pb and Co. Among its other uses, the most interesting is the reaction with fluoride.

Belcher *et al.* [109,110] discovered that its red complexes with cerium(III), lanthanum, praseodymium, and to some extent also samarium, produced blue water-soluble complexes with fluoride ions. The reaction is generally regarded as the only colour reaction of the fluoride ion (although another has recently been proposed [111]).

Leonard and West [112] attribute the blue colour to a ternary complex with fluoride. The normal cerium complex has the structure (I), the ternary complex structure (II).



This reaction has been extensively studied and applied.

The prize examples of reactions with high sensitivity and specificity are perhaps those of chemiluminescence and bioluminescence. Chemiluminescence measurements are highly specific compared with conventional techniques such as coulometry and colorimetry [113]. A limited number of such reactions are known at present, but they have great utility in practice.

known at present, but they have great utility in practice.

Chemiluminescence is a characteristic feature of the reactions of ozone with many inorganic and organic materials. Thus Regener [114,115] utilized the intense emission from the reaction between ozone and Rhodamine B, adsorbed on an activated silica gel surface, in the first chemiluminescence detector for atmospheric ozone. This procedure was utilized by the Environmental Protection Agency (EPA) for monitoring ozone in polluted atmospheres [116]. An automated version of this analyser is commercially available.

A homogenous gas-phase chemiluminescence technique for the detection of ozone was reported by Nederbragt *et al.* [117]. The detector employed a chemiluminescence reaction at atmospheric pressure between ozone and ethylene. The intensity of the emission ( $\lambda_{\text{max}} \sim 435$  nm) is directly proportional to the ozone concentration. The detector responds linearly to ozone concentrations between 0.003 and 30 ppm, and no interferences have been observed.

The reaction between ozone and nitric oxide in the gas phase yields chemiluminescence in the infrared region and may be used for detection of either reactant [118]. It is the principal reaction used in the detection of oxides of nitrogen. The reactions involved are

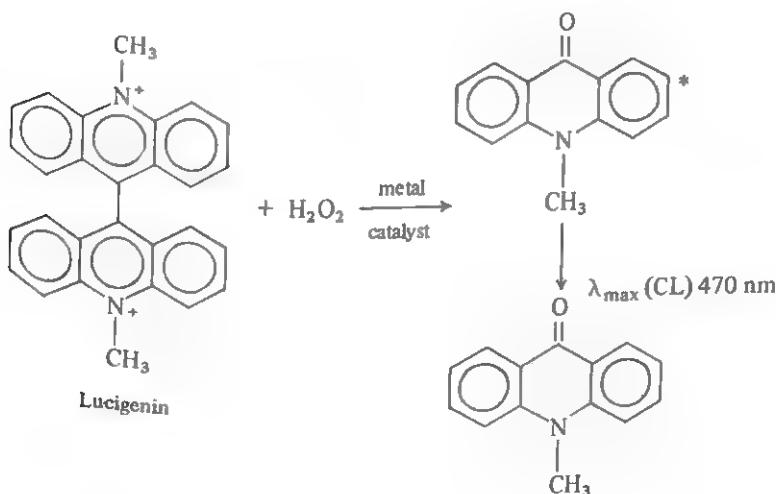


and the mechanism and kinetics have been described by Clough and Thrush [119]. The direct chemiluminescent reaction is applicable only to the detection of NO. For detection of  $\text{NO}_x$  ( $\text{NO} + \text{NO}_2$ ), prior conversion of  $\text{NO}_2$  into NO is required.

These examples show the utility of chemiluminescent reactions in the selective determination of air pollutants.

Instrument manufacturers have capitalized on these developments and now offer a family of monitors capable of monitoring sulphur dioxide, hydrogen sulphide, oxides of nitrogen and ozone by means of chemiluminescence reactions.

Another interesting reaction is that with participation of lucigenin [120], the chemiluminescence (CL) being used for determination of hydrogen peroxide or trace metals.



Lucigenin is similar to luminol in giving chemiluminescence when oxidized by peroxide in basic solution in the presence of metal ion catalysts.

The bioluminescence system of the firefly has been the most studied. It is summarized in the following scheme:



where  $\text{LH}_2$  = luciferin;  $\text{E}$  = luciferase;  $\text{ATP}$  = adenosine triphosphate;  $\text{AMP}$  = adenosine monophosphate;  $\text{PPy}$  = inorganic pyrophosphate.

The bioluminescence (BL) efficiency of this reaction is generally unity. When this reaction is carried out with ATP as the analyte, the detection limit is 0.1–1.0 picomole, with linearity of response over five orders of magnitude.

Some investigators, taking extreme care, have been able to detect the ATP in a single bacterium, i.e.,  $2 \times 10^{-5}$ – $1 \times 10^{-2}$  picomole. The difference in these two detection limits arises from contamination of the reactants with ATP, or presence of the interferent AMP in the ATP extract.

The bacterial system follows the firefly system in popularity for study. The following reactions schematically represent the bacterial system.

The overall reaction is suggested to be:



which is thought to be the sum of reaction series A and B.

Series A



$\text{FMN}$  = flavin mononucleotide.

Series B



The BL efficiency for this reaction is about 0.05. The intensity of the emission depends on the chain-length of the aldehyde.

Bacterial BL has high specificity for FMN. Some substituted FMNs and flavin adenine dinucleotide (FAD) also react with bacterial luciferase (E) to produce light but the level of emission is low enough to be of little analytical concern.

The relationship between light output and  $\text{FMNH}_2$  concentration is linear from  $1.0 \times 10^{-4}$  to  $1.0 \mu\text{g}/\text{ml}$ .

The BL assay for FMN is applicable to many of the same systems as the ATP method. It has been used to monitor infectious bacteria and has been extensively investigated as a possible detector of extraterrestrial life.

The dependence of the bacterial BL on  $\text{FMNH}_2$ , and the participation of FMN in the reaction



where  $\text{E}' = \text{NADH dehydrogenase}$ , leads to the possibility of analyses which do not depend directly on FMN but on some substrate being oxidised by NADH or reduced by  $\text{NAD}^+$ .

For example, a method for nitrate could be based on the reactions:



The concentration of the resulting  $\text{FMNH}_2$  is proportional to the initial nitrate concentration.

These examples show the extreme importance of the analytical reactions of chemiluminescence and bioluminescence in terms of their operational parameters and the wide possibilities for their utilization in practice.

The schemes shown above also illustrate the importance of knowledge of the reaction mechanism, which in many cases is not simple.

To conclude this section, we shall describe a group of reactions used in a series of methods less well known by analysts but widely utilized by biochemists. These are the reactions used in immunological methods of analysis. These methods have gained considerable importance during the past few decades because of their high specificity and sensitivity. They are based on the formation of a complex between antigen and antibody. They all originate from the basic research work on human immunoreactions carried out by Behring, Pasteur and others [80].

During recent years the technique of radioimmunoassay (RIA) has gained wide acceptance as a sensitive ( $\text{ng}/\text{ml}$ ) and very specific analytical method for biological compounds. Originally described by Yalow and Berson [121] as a

procedure for the detection of insulin in human plasma, the radioimmunoassay technique was soon extended to almost all compounds that can directly stimulate specific antibody development in animals or can be made immunogenic as haptens. This technique introduced a new era in endocrinology [122].

The applications of radioimmunoassay and related techniques such as competitive protein-binding, radioenzymatic, radioreceptor, and immunoradiometric assays, are now no longer restricted to endocrinology.

This method has become absolutely necessary, especially in those cases where the conventional procedures are not sensitive enough to be usable.

The materials assayed include protein and non-protein hormones, vitamins, nucleic acids, enzymes, drugs, metabolites, cancer antigens, viral antigens, antibodies, and structural proteins. The procedures are used for drug tests on athletes, particularly for tests for steroids.

Figure 2.8 gives the principle of radioimmunoassay [123].

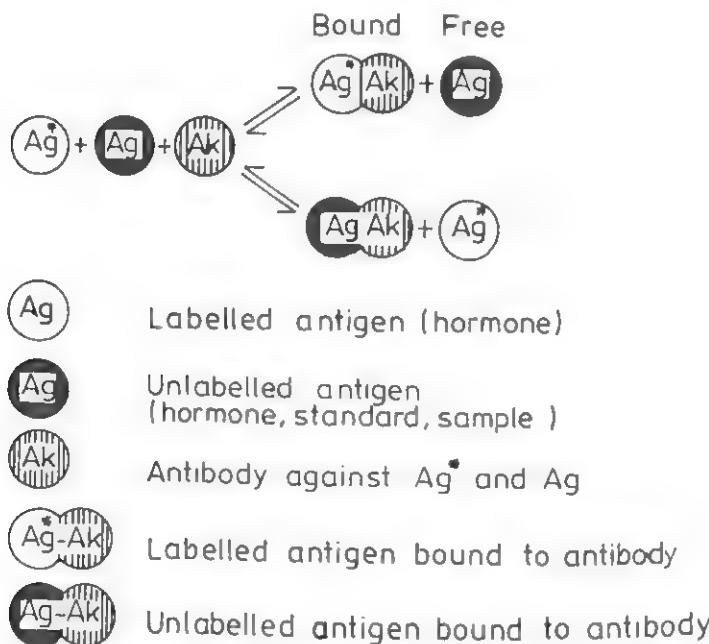


Fig. 2.8 Principle of radioimmunoassay [123] (by permission of the copyright holders, Die Medizinische Verlagsgesellschaft Marburg).

The considerable importance of these extremely specific methods is shown by the number of publications ( $>1000$ ) each year.

From this short examination of some types of reactions, we can draw some conclusions important for the future specialist or teacher in analytical chemistry.

(i) Reaction chemistry is a multidisciplinary topic involving analytical, inorganic, organic, and physical chemistry, especially the first. For these reasons,

analytical chemistry *must* be studied since it correlates basic knowledge in the other three domains.

(ii) Irrespective of the development of analytical instruments, study of chemical reactions is essential for an analyst. An automated analytical instrument can be handled under prescribed working conditions even by a non-expert, but the conditions themselves can only be established by the specialist who understands how the 'black box' functions, the nature of the analytical problem, and how to apply the one to the other.

To produce analytical chemistry, the analyst must know chemistry, just as a musician playing an instrument must know and understand the relation between musical notes and the method by which they are produced.

Teaching in analytical chemistry must therefore necessarily take into consideration the study of chemical reactions.

(iii) Special attention must be paid to the way in which new reactions must be examined in order to optimize the operational parameters to minimize the effects of competitive reactions. In this way 'analytical' thinking can be inculcated, and the production of mere 'number-generators' can be avoided.

(iv) The future analyst must be familiarized with the study of reaction mechanisms. Such a study, irrespective of the nature of the reagents, has a pronounced analytical content. This domain of analytical chemistry is in our opinion fascinating, being the key to all analytical methods.

(v) The importance and significance of the sensitivity of a reaction must be properly understood.

With regard to sensitivity, we quote Hirsch [124]: "In analysis, the signal must be defined in relation to two other factors, the background and the noise, and here also I feel that the distinction is not always made clear in analytical courses. The concept of limit of detection is also part of the idea of a signal".

## 2.2.2 Instrumental

"To research means to see what all people have seen and to think what nobody has thought" [125]

### 2.2.2.1 General Considerations

Analytical chemistry, as an independent science, deals with the theory of analytical procedures, and with the materials and problems to which they are applied.

Any analytical determination is based on the correlation between some physical property ( $P$ ) and the amount (usually expressed in terms of concentration,  $C$ ) of the species to be determined.

This may be represented by the expression

$$P = f(C)$$

which indicates the extremely wide scope of physical methods of analysis.

The terms classical and modern methods of analysis, or chemical, physico-chemical, or instrumental methods of analysis, although useful and well understood, in a sense create false barriers within analytical chemistry, since *all* methods involve the use of some kind of measuring instrument, whether it be a balance, a burette, a spectrophotometer or a scintillation counter. Thus in this sense all methods are physical (or instrumental) methods [126].

If we use the terminology of automation, we may divide the operation scheme of an analytical process into three steps, irrespective of the type of method:



All research in analysis, whether on laboratory or on-line methods, should have as its aim the improvement of the correlation between these three steps in order to provide the most reliable and sensitive analytical signal within the shortest analysis time.

The student of analytical chemistry must be made familiar with this point of view, the basic philosophy of analysis, right from the start.

Because of the importance of this, the third chapter of this book will discuss these steps. Here we shall confine our attention to the question of what is commonly referred to as instrumental analysis, taking it for granted that classical methods and reaction chemistry have already been properly taught, as emphasized above.

The problem for an analytical chemist is always basically the same: to find the most appropriate method of analysis, choose the conditions so that correct and useful information is obtained, and to do all this as economically as possible.

Foreman and Stockwell [127], in discussing automation, remark: "For each problem the following possibilities must initially be considered:

- (a) is a commercial instrument available to perform the analysis?
- (b) can any commercial instrument be modified to perform the analysis?
- (c) if neither (a) nor (b) applies, can the design and development costs involved in automation be justified in cost-benefit terms?

An affirmative answer to (c) generates an applied research project to design, build, and test an automatic analyser. Research in automatic analysis ideally requires a multi-disciplinary team including specialists in chemistry, physics and electronics, in addition to an adequate degree of engineering support."

To see how this philosophy is applied in the rapid gathering of good quality analytical information, we must consider the relation of method to instrument and of man to instrument.

#### *2.2.2.2 The Method and Instrument Relationship*

First let us see what is meant by an instrument.

McKee [128] says: "Simply stated, all instruments have three parts: input

transducer, signal transformation modules, and output transducer. The input transducer, or detector, responds predictably to the physical property to be measured. The signal transformation modules perform necessary and/or desirable operations on the electrical output from the detector. The output transducer converts the final electrical signals back to physical ones we can read and interpret. With the addition of a reference signal on a feedback loop, an instrument becomes a control system".

This is illustrated in Fig. 2.9.

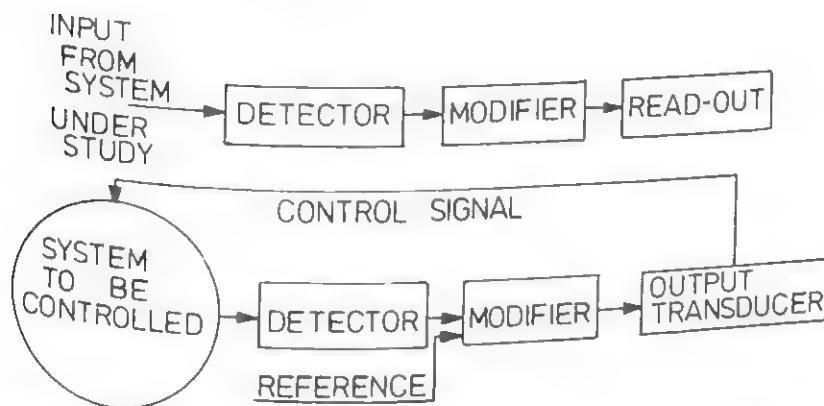


Fig. 2.9 Top, instrument. Bottom, control system [128]. (Reprinted with permission from *Anal. Chem.*, 1970, **42**, No. 11, 91A. Copyright by the American Chemical Society.)

The signal from the detector is compared with the reference. The output modifier is then used to operate some device which will cause a change in the physical system and reduce the difference to zero.

The simplest example of the method-instrument relationship is the dependence of gravimetric methods on the balance. Irrespective of the chemical nature of a gravimetric method, the final result depends on weighing on a balance. The balance has undergone continued improvement. In an excellent article 'Weighed in the balance', Stock [129] says "The history of balances is really the history of the development of the bearings and the beam of the two-pan balance to assure both sensitivity and precision".

The same example shows very well that a given combination of method and instrument may not be adequate for a particular purpose, and a different combination must be used. Thus gravimetric methods would be useless for determination of trace metals in a single drop of blood. On the other hand they are ideal for very precise analysis for major components of large samples. where many 'instrumental' methods would be less satisfactory. In other words, the right tool must be chosen for the job - hammers should not be used as screwdrivers, and the right size and type of screwdriver must be selected.

We must remember that the instrument has to be integrated in an ensemble, whether it is operated manually or automatically, the ensemble being the total analytical 'black-box'.

Gravimetric analysis again provides an example, in thermal analysis. Modern instruments for thermogravimetry permit the use of very small samples ( $\sim 1$  mg), controlled atmospheres, remote control, computerized data-processing, analysis of products, etc. [130] but may also be used in the same way as the earliest thermobalances.

Another illustration can be drawn from the various polarographic techniques. It took many years from its discovery by Heyrovský for polarography to realize its full potential. Indeed, at one stage it was even asserted that polarography was obsolete as an analytical method. New techniques were developed, however, the instrumentation was improved, and new applications were found. Hence Flato [131] can remark: "Thus, we see a technique which is one of the oldest instrumental techniques available and which fell into disuse as the newer techniques came along, now returning to a place of prominence in the analytical laboratory, finding its way into new applications where it has previously not been tried, and owing to the availability of modern instrumentation, returning to its rightful place in the laboratory".

To emphasize this, Table 2.12 shows the detection limits of selected electroanalytical methods [132].

**Table 2.12**

Sensitivity limits of selected electroanalytical methods [132]  
(by permission of the copyright holders, Akadémiai Kiadó, Budapest).

Method	Sensitivity limit ( $M$ )
Classical polarography	$5 \times 10^{-6}$
Chronopotentiometry with various current programmes	$10^{-5}$
A.c. polarography (voltammetry)	$10^{-5}$
Linear scan voltammetry	$10^{-6}$
Rotating disk voltammetry	$10^{-6}$
Phase-sensitive a.c. polarography	$10^{-7}$
Second harmonic a.c. polarography	$10^{-7}$
Charge step polarography	$10^{-7}$
Polarography with alternating triangular voltage	$10^{-7}$
Square-wave polarography	$5 \times 10^{-8}$
Normal pulse polarography	$5 \times 10^{-8}$
Differential pulse polarography	$5 \times 10^{-8}$
R.F. polarography	$5 \times 10^{-8}$
Anodic stripping with HMDE	$10^{-10}$
Anodic stripping with thin-film electrodes or solid electrodes	$10^{-11}$

Another example is that of flame photometry and atomic-absorption spectrophotometry.

The study of the flame was initiated by Bunsen and Teclu, and has resulted in two complementary analytical techniques of high sensitivity and selectivity, reasonable precision, and adequate speed.

The appearance of the first flame photometer produced a revolution in analytical techniques for alkali or alkaline-earth metals, which required considerable skill for determination by classical methods. Flame photometry is limited to those elements which can be adequately excited at flame temperatures. With increase in these temperatures by use of more sophisticated gas mixtures, the number of determinable elements has increased, though it is still limited.

With the passage of time, flame photometry has been complemented and in some applications superseded by newly developed techniques such as atomic-absorption and atomic-fluorescence spectrophotometry.

The phenomenon of atomic absorption was discovered by Fraunhofer in 1814 but it had to wait 140 years before Walsh put it on a practical footing. He realized that for a readily measurable signal to be obtained the width of the line of the excitation radiation would have to be narrower than that of the resonance absorption line, and also developed the means of ensuring this. This new technique brought many advantages (high sensitivity and unusual selectivity, coupled with good performance) and now covers a wide range of elements as well as being applicable to indirect determination of some anions.

In the first ten years from its development in 1954, there was enormous expansion of research in this field, and it was considered that the performance limits of atomic absorption had already been reached. However, the studies by L'vov, West and Massmann led to new techniques in atomic absorption, with still higher performance (electrothermal atomic absorption). The absolute detection limit of such techniques for some elements (Cd, Zn) is as low as  $10^{-14}$  g, comparable with that of the radiometric or electron-microprobe methods.

It is also interesting to compare the way in which two of the separation techniques complement each other, namely gas chromatography (GC) and high-pressure liquid chromatography (HPLC). Each has a well-defined field of application, and they cover between them the majority of inorganic, organic and organometallic compounds.

Gas chromatography is restricted to sample components, or readily made derivatives of them, that are sufficiently volatile at temperatures below their decomposition temperature or that give strictly reproducible pyrolysis behaviour with a given temperature regime.

Research in gas chromatography has been mainly concerned with the development of columns and their manipulation (heart-cut, back-flush, temperature programming) and of detectors of greater sensitivity and selectivity.

The enormous analytical potential of the combined gas chromatograph/mass spectrometer was quickly realized in 1957 when Holmes and Morrell [133]

reported their rudimentary coupling of the two instruments with a stream splitter as an interface [134]. The mass spectrometer is a universal detector in gas chromatography, since any compound that can pass through the chromatograph will be converted into ions in the mass spectrometer. At the same time the highly specific nature of mass spectra makes the mass spectrometer a highly specific and also sensitive detector in gas chromatography.

To demonstrate this, Table 2.13 gives the sensitivity of various detectors [134].

**Table 2.13**

Sensitivity of GC detectors [134]

(Reprinted with permission from *Anal. Chem.*, 1977, 49, 447A.

Copyright by the American Chemical Society.)

Total ion current monitoring	$10^{-8}$ g
Mass chromatogram	$10^{-8}$ g
Flame ionization	$10^{-9}$ g
Electron capture	$10^{-12}$ g
Selected ion monitoring	$10^{-12}$ g

Perhaps the most intriguing aspect of the mass spectrometer as a detector is its great versatility, since it can provide scanned spectra, mass chromatograms, resolved total ion-current chromatograms, and record selected ions, etc., with variable mass resolving power, and an ever-growing selection of ionization techniques [134].

HPLC has simply increased the speed of separation in liquid-liquid chromatography and is most suitable for the compounds that are insufficiently volatile or too thermally labile for gas chromatography to be successful. It has proved of great utility for the separation of a wide variety of organic compounds with complex structures, thermally degradable compounds, pharmaceutical products, intermediate products in synthesis, and physiologically active products.

Both GC and HPLC give high performance in the sense of enormous versatility in application, and high sensitivity and selectivity. HPLC, as a new technique, is continuously being improved by the development of a wide variety of detectors, the most popular being multiwavelength absorption, fluorescence and electrochemical (amperometric and coulometric) [135]. As with most instrumental methods, improvement in reproducibility tends to lag behind other developments.

The coupling of different chromatographic techniques with other instrumentation has led to spectacular results. It is possible to collect complete analytical information about a complex mixture of suitable components, by using HPLC with a microprocessor and a computer (Hewlett-Packard or Du Pont), in only a few minutes.

The words of Paul Karrer, Nobel Prize co-winner in Chemistry (1937), at the 1947 IUPAC Congress [136], are still valid: "No other discovery has exerted as great an influence and widened the field of investigation of the organic chemist as much as Tswett's chromatographic adsorption analysis. Research in the field of vitamins, hormones, carotenoids and numerous other natural compounds could never have progressed so rapidly and achieved such great results if it had not been for this new method, which has also disclosed the enormous variety of closely related compounds in nature".

When the method is completely suited to the instrument, on-line analysis becomes possible. In our opinion, the student or research worker should have the opportunity to use almost all types of laboratory instruments and to be acquainted with the automatic systems used for control of the technological processes in the chemical industry.

The most frequently used technique in automatic analytical control is process gas chromatography. The object of installing analysers on-line is to obtain analytical results at a speed comparable to that of changes in the process, and to use the information to take corrective action through a feed-back loop.

A process gas chromatograph is an instrument designed to fulfil this aim and operates on-line continuously, giving automatic repetitive analysis of a flowing process stream. It is usually dedicated to a particular analysis on a single stream, or at most, a few streams (multistream analysis), and is designed to measure one or, at most, only a few of the components in the sample [137]. The sample loop and chromatograph must be situated as close to each other and the process vessel as possible, to minimize transport times.

The mode of use of process gas chromatography depends on the technological process. The commonest applications are in open- or closed-loop process control. In open-loop systems the operator adjusts the process conditions on the basis of the chromatographic results. In closed-loop control the changes are made automatically, usually through linkage to a computer.

Table 2.14 lists some of the principal uses of on-line chromatographs [137]. From a poll of readers of the journal *R/D*, Thomas [138] reported that for the sixth successive year, liquid chromatography led all analytical instrumentation in growth rate (planned acquisition divided by present use). This illustrates both the competition between various techniques of analysis and the continued importance of chromatography. Figure 2.10 gives Thomas's findings [138] for 32 types of analytical instruments and equipment. The growth rate is calculated with present users as the base, for each instrument category. The total number of users includes all who plan to acquire; new users are those who do not presently use that particular instrument but who plan to acquire one. The difference is the number of present users planning to acquire additional instruments or equipment.

This study also shows very strong growth rates for particle size analysers and ion-selective electrodes.

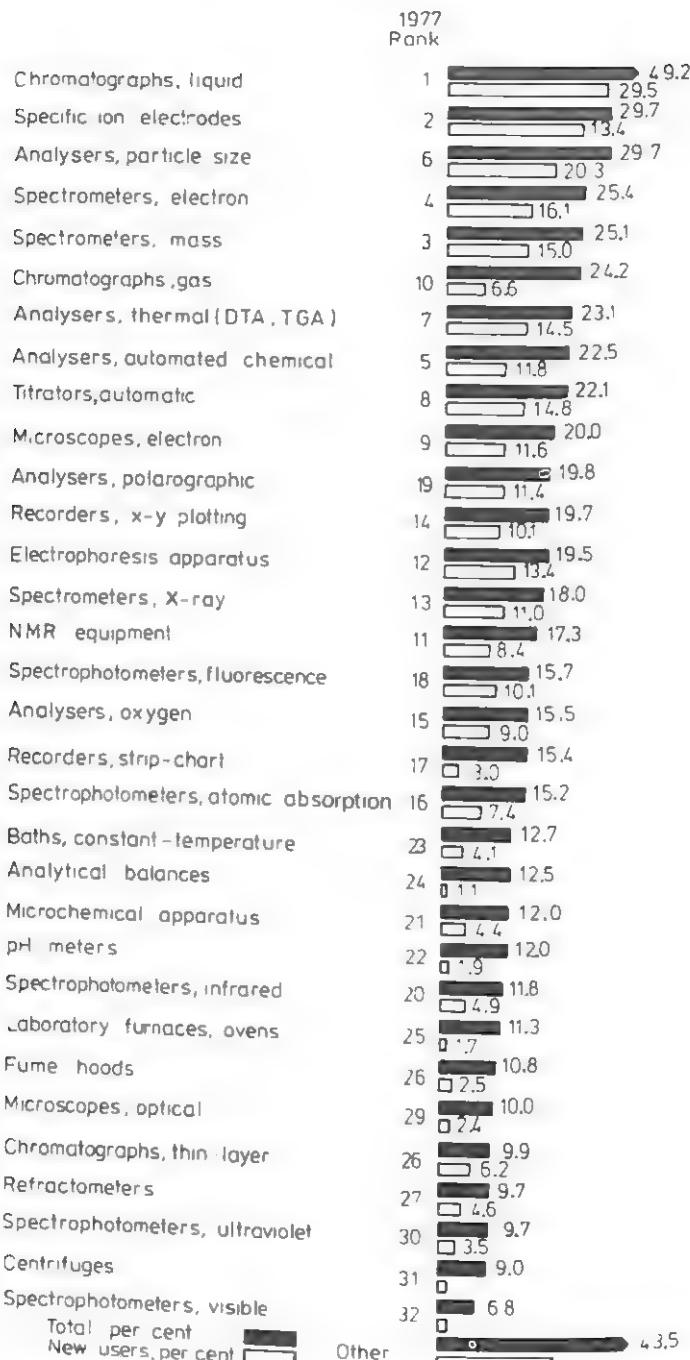


Fig. 2.10 Growth rate of various instruments [138] (by permission of the copyright holders, Technical Publishing Co., Barrington, USA).

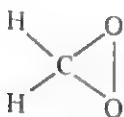
Table 2.14

Principal uses of process gas chromatographs [137].  
 (Reprinted with permission from *Anal. Chem.*, 1975, 47, 983A.  
 Copyright by the American Chemical Society.)

- Process Control – Use information to adjust process through open- or closed-loop control
- Process Study – Obtain information about process, to improve yield or throughput. Correlate process variables with product quality
- Process Development – Obtain information about process characteristics, as in pilot plants. Correlate process variables with reaction products and yields
- Material Balance – Use information to calculate material balance for process units
- Product Quality Specification Monitor – Monitor impurities in outgoing or incoming product for conformance to specifications
- Waste Disposal Monitoring – Monitor liquid or gas effluent wastes for loss of valuable product or for presence of toxic compounds
- Personnel Safety-Area Monitoring – Monitor ambient air for presence of toxic compounds

### 2.2.2.3 Man and Instrument

The January 1978 issue of *Analytical Chemistry* carried an article describing the discovery (at the National Bureau of Standards, NBS) of a simple molecule, dioxirane, believed to play an important role in the formation of photochemical smog [139].



Dioxirane

The reaction under investigation was that between ozone and ethylene. In the first step, mass spectrometry was used to study the reaction of gaseous ozone and ethylene. Microwave spectrometry was used to try to identify the reaction products.

The microwave absorption spectrum and subsequent isotopic substitution experiments established that the compound was indeed dioxirane, as independently deduced earlier from a computer study of model schemes.

After the identification of dioxirane by microwave spectrometry, a set of temperature-controlled experiments was performed, and mass spectrometry

confirmed the presence of an unstable species, the mass of which corresponded to that of dioxirane.

This example of the discovery of a molecule that looks unlikely to exist, constitutes a conclusive proof of the importance of interaction between man and instrument. To discover the molecule, high-performance techniques and advanced equipment were needed, but only a sufficiently intelligent group of research workers could have combined them. This example is also a very good illustration of the fact that analysis is essentially a problem-solving science [140, 141].

It is evident that in the relation between man and instrument it is man who thinks, and even an instrument endowed with a memory can think in only an elementary manner. The scientist can never be compared with a machine or substituted by it.

Wiener says "If it is an offence against our self-pride to be compared to an ape, we have now got pretty well over it; and it is an even greater offence to be compared to a machine" [142].

No matter how much an instrument may be improved, it cannot surpass the capabilities of the human intelligence, cannot have the same ability for diverse decision-making as its operator.

Wiener also comments: "Thus one of the great future problems which we must face is that of the relation between man and the machine, of the functions which should properly be assigned to these two agencies. On the surface, the machine has certain clear advantages. It is faster in its action and more uniform, or at least it can be made to have these properties if it is well designed. A digital computing machine can accomplish in a day a body of work that would take the full efforts of a team of computers for a year, and it will accomplish this work with a minimum of blots and blunders.

On the other hand, the human being has certain nonnegligible advantages. Apart from the fact that any sensible man would consider the purposes of man as paramount in the relations between man and the machine, the machine is far less complicated than man and has less scope in the variety of its actions" [142].

The relation between man and instrument has been for a long time the concern of many thinkers, even when instruments had much more limited performance, automation or computerization than they do now. Civilized man has always tried to build instruments to further his work, and his research, but an intelligent man never makes a fetish of instrumentation. He uses it to ease his work, and to increase the rate of obtaining information.

Goethe describes very well, in *Faust*, man's attitude towards instruments. In the first part of the tragedy, Faust is represented as a physicist in his work-room surrounded by laboratory instruments. He says [143]:

Ye instruments, forsooth, but jeer at me  
With wheel and cog, and shapes uncouth of wonder:  
I found the portal, you the keys should be;  
Your wards are deftly wrought, but drive no bolts asunder!

Mysterious even in open day.  
Nature retains her veil, despite our clamors:  
That which she doth not willingly display  
Cannot be wrenched from her with levers, screws, and hammers.

Faust's wish for deeper knowledge makes him accept an agreement with the devil.

This fragment illustrates Goethe's attitude towards the world of science. He understood that progressive change of human society depends on correlation of natural sciences and technical means. The progress of science cannot be stopped, evolution is irreversible. Goethe understood that, but he was anxious about the future [144].

We see today the appearance of the 'third generation' of laboratory equipment, practically completely automated thanks to microprocessors. The analytical signal appears in the most suitable form and automation of different types of instruments, pH-meters, atomic-absorption equipment, spectrophotometers, gas and liquid chromatographs, etc., makes the output signal objective, eliminating many of the errors due to the operator, for example the errors in introducing very small samples, as in GC or HPLC.

In spite of the advantages of present instrumentation, however, there are some difficulties inherent in such sophisticated devices. With some exceptions, the beneficiary of the output signal, the analytical chemist who handles the instrument, has a limited knowledge of the electronic or mechanical construction of the instrument, and may be uncertain of the reliability he can place on the signal. Further, remedying any faults that may develop in very sophisticated instruments needs highly qualified specialists.

In many laboratories, in order to avoid this problem with high-performance equipment, someone is specially trained to work with an instrument and to handle it under optimal conditions. Doing so, however, though protecting the equipment and its performance, may perturb the interaction between man and instrument, since a tendency arises for the specialist to become the slave of the instrument and also to believe it has universal scope. To solve the complex problems of analytical chemistry, the analyst must understand that the apparatus constitutes only the means of obtaining the desired analytical information. He must adapt his analytical methods to the instruments available, using a variety of approaches to be sure of the analytical information.

To conclude this section, we cite from a recent Romanian book 'Man and the Informational Universe' [145]: "Electronic devices for information processing cannot become neurasthenic. If man were simply an informational machine (in the engineering sense of information), he could not suffer from mental illness. Would men be willing to become machines to obtain this benefit? It is nonsense to speak of neurosis of a machine, even of an electronic computer, because the machine cannot become estranged from other machines. The neurasthenic suffers because he feels isolated from the world. He lives the tragedy of an estranged

being only because he feels that he is alone". ... "Schizophrenic communication has no code and therefore cannot be deciphered. No other illness, whether physical (oligophrenia or dementia) or neurological (aphasic imagery) illustrates so obvious semantic or informational pain, as schizophrenia".

## 2.3 DATA PROCESSING

### 2.3.1 Data Domains

As we have shown, present-day laboratory equipment has profited from the development of electronics, increasing the measuring rate, accuracy and convenience, while decreasing the instrument size and power requirement. Integrated circuits and hybrid circuits have brought many measurement techniques from the realm of theoretical possibility to reality.

The role of the equipment is to obtain from the measured system the desired information, and make it accessible as a signal irrespective of its form.

Owing to the continuous development of laboratory instruments, with electronic circuits very frequently misunderstood by the chemist, it was necessary to find a means of applying new devices efficiently and effectively, the only requirement being an understanding of the basic measurement concepts.

In the design, analysis, description and modification of such electronic equipment, the signals of different types are classified in 'data domains'. A much better understanding of the data-handling process is gained as a result of the study and application of the data-domain concepts. These are given below, together with some basic concepts concerning measurement devices [146].

#### *Data Domains*

1. Measurement data are represented in an instrument at any instant by a physical quantity, a chemical quantity, or an electrical signal. These quantities which represent the measurement data can be categorized in groups called 'data domains'.

2. As the data proceed through the instrument, a change in the equivalent quantity is called a 'data domain conversion'.

3. All electronic measurement systems can be described as a sequence of two or more data-domain converters; the logic of each can be analysed separately.

4. Methods of using electrical signals to represent measurement data fall into three major domains: analogue, time, and digital.

#### *Measurement Devices*

1. All measurement devices employ a difference detector and a reference quantity.

2. The difference detector and/or the reference can affect the accuracy of the measurement.

3. The reference must be identical in nature with the characteristic being measured.

4. Interdomain converters have the characteristics of measurement devices.

### 2.3.1.1 Analogue, Time and Digital Domains

For the teacher of 'modern' analytical chemistry there are difficulties in being up to date in teaching this discipline, because of the method-instrument relationship, which is difficult for students to perceive and realize.

However, to help chemists and analysts, books on electronics have been specially written for scientists and chemists. The book by Malmstadt and Enke [147] is already a classic in terms of applicability and quality.

In our opinion a recent Romanian book 'Electronics for Chemists' [148] also achieves this aim. It describes simply and clearly the functional principles of laboratory equipment, in a manner which may be understood by any chemist.

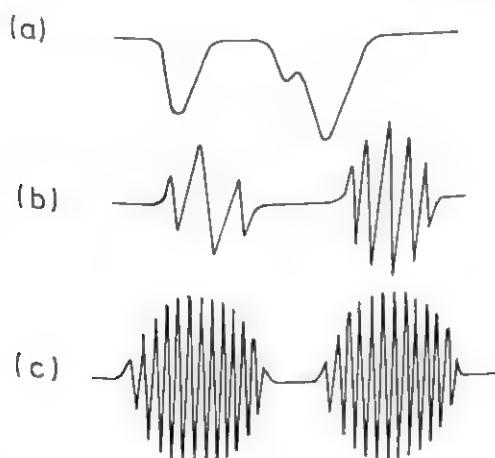
We shall give in the following some of the definitions from these books, concerning the analogue, time and digital domains.

The *analogue domain* contains signals which may vary continuously. The observed quantity is represented by the signal amplitude, the variation of which may be plotted against time, wavelength, magnetic field strength, temperature, or other experimental parameters.

Most transducers convert physico-chemical quantities into the analogue domain. For example, electrodes convert pH into a potential, photodetectors convert radiation intensity into an electric current.

Figure 2.11 shows some analogue ( $E_A$ ) domain signals [146].

In the *time domain* the measurement data are given by the number of events in unit time, not by the variations in signal amplitude. This involves the existence of two levels of magnitude for a signal (e.g. on-off, high-low). A given quantity coded in this domain is characterized by the number of changes between these



— TIME, WAVELENGTH, FIELD STRENGTH, ETC.—

Fig. 2.11 Analogue ( $E_A$ ) domain signals [146]. (Reprinted with permission from *Anal. Chem.*, 1971, **43**, No. 1, 69A. Copyright by the American Chemical Society.)

levels in a given time interval (i.e. a frequency or pulse-rate) or by the time elapsed between two consecutive changes (pulse-time).

The minimal time for a measurement in this domain is the pulse time. The signal amplitude no longer has the same significance as in the analogue domain. The higher the rate of change in the signal, the greater the timing precision or the precision of measuring the information contained in the signal. Examples of transducers which generate coded signals in the time domain are the Geiger-Muller counter, which produces a pulse-rate proportional to the level of radioactivity, and the piezoelectric oscillator, which changes frequency with temperature.

Figure 2.12 shows some time ( $E_{\Delta t}$ ) domain signals [146].

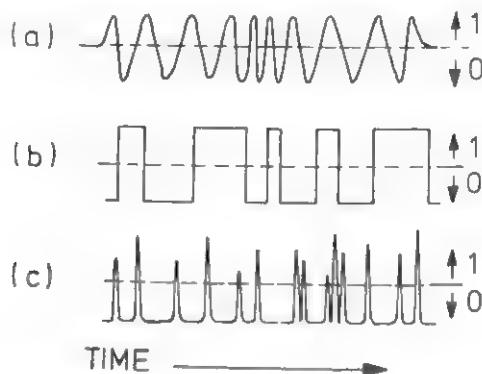


Fig. 2.12 Time ( $E_{\Delta t}$ ) domain signals [146] (Reprinted with permission from *Anal. Chem.*, 1971, 43, No. 1, 69A. Copyright by the American Chemical Society.)

In the *digital domain*, the measurement data are contained in a two-level signal coded to represent a specific integer (or character). The signal may be a coded series of pulses in one channel (serial form) or a coded set of simultaneous signals in multiple channels (parallel form).

In Fig. 2.13 some representative digital signal waveforms are shown [146].

The serial count waveform (a) represents the number of pulses in a series with a clearly defined beginning and end. This type of signal is simple but not very efficient. The most efficient serial digital signal is the binary-coded signal (b), where each pulse time in the series represents a different bit position in a binary number. The appearance of a pulse indicates a 1; the absence of a pulse, a 0.

The binary-coded decimal serial form is not so efficient but very convenient when a decimal numerical output is desired. Each group of four bits then represents one decimal digit in a number, so twelve bits can represent a three-digit decimal number and provide a resolution of one part per thousand.

A parallel-form digital signal uses a separate channel for each bit position instead of a separate time in a single channel. Its principal advantage is speed. Figure 2.13(d) shows an 8-bit parallel data-source connected to indicator

lights to show the simultaneous appearance of the data logic levels on all eight channels.

Various coding systems are used for parallel digital data. The parallel system is used in all modern fast computers. The serial system is often used for telemetry and slow computer peripherals such as teletypes.

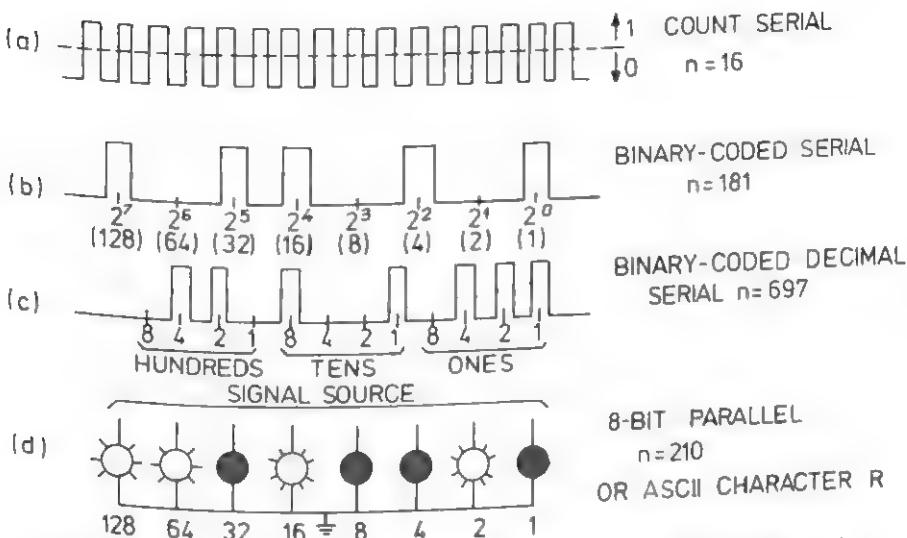


Fig. 2.13 – Serial and parallel digital signals [146]. (Reprinted with permission from *Anal. Chem.*, 1971, 43, No. 1, 69A. Copyright by the American Chemical Society.)

### 2.3.1.2 Mapping Domain Conversions

A measurement involves a series of conversions between domains, such as conversion of hydrogen activity into an electrical potential. This sequence of conversions may best be followed by means of a plot or 'map' of the given data domain. Modern laboratory instruments frequently use three or more domain conversions to perform the desired measurement. When analysing the conversions in an instrument it is helpful to use the data domains map shown in Fig. 2.14 [146].

Such a map does not have a fixed structure, the division of the circle into sectors depending on the particular apparatus. The upper semicircle represents the non-electrical quantities, i.e. the physical and chemical quantities which may characterize a certain system, and are finally converted for the operator's use, e.g. the position of an indicator needle on a scale. The lower semicircle represents the electrical quantities, grouped into the analogue, time and digital domains. The path of the signal can be traced out on the map as it is followed through the instrument.

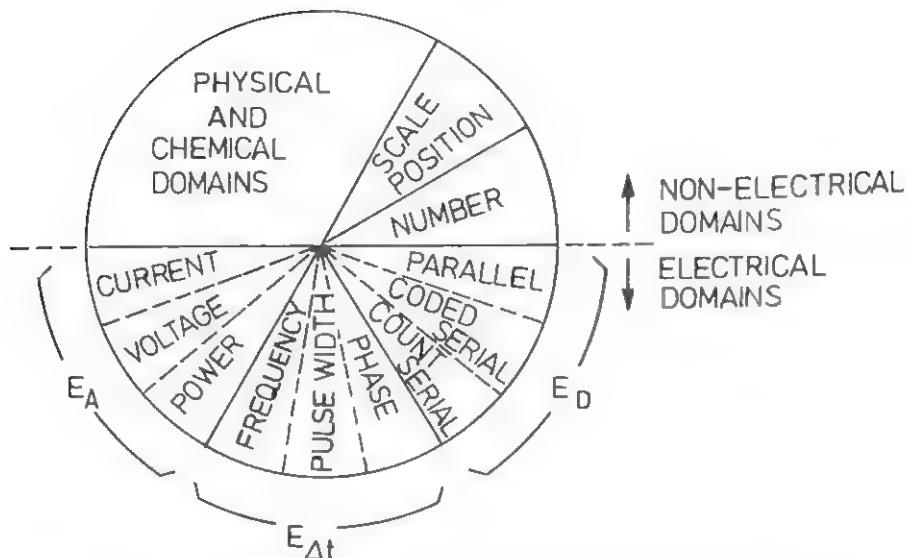


Fig. 2.14 – Data domains map [146]. (Reprinted with permission from *Anal. Chem.*, 1971, 43, No. 1, 69A. Copyright by the American Chemical Society.)

### 2.3.2 Informational and Statistical Treatment of Data

According to Kowalski [149], the informational and statistical treatment of data constitutes an independent discipline, called chemometrics. Chemometrics includes the applications of mathematical and statistical methods to the analysis of chemical measurements.

In this discipline, a primary role is played by pattern recognition.

The objective of pattern recognition is to characterize objects (in our case the different chemical compounds) by measurements, and to study relationships based on similarities among the objects. Pattern recognition methods operate with defined criteria and attempt to distil useful information from raw data.

Probably the most important area of future development is the incorporation of pattern recognition methods into on-line measurement systems. A useful review is given by Kryger [86].

Modern mathematical statistics began to develop on the basis of the theory of probability at the turn of the twentieth century. Chemical analysis provides one of its most important fields of application.

“The existence of the multitude of new physical methods of analysis urgently raises the question of finding rational criteria for comparing the results obtained by various analytical methods. The development and introduction of new analytical methods take place considerably faster than their standardization. It is already evident that an analyst must be as thoroughly familiar with the methods of modern mathematical statistics as the geodesist with the method of least squares” [150].

Chemists using pattern recognition methods, as well as optimization, factor analysis, and several other chemometric methods, are demonstrating that the computer is capable of aiding significantly in providing better and more useful chemical information with less effort expended by the chemist.

### 2.3.3 Applications of Digital Computers in Analytical Chemistry

As Dessy says [151] "The art of analytical chemistry is being altered by the impact of computer technology".

Digital electronics and laboratory-scale digital computers are steadily moving towards a dominant position in the design of laboratory instruments and it is likely that they will become an indispensable part of much laboratory experimentation. Computers have also come into use for rapid data reduction during analysis.

During the 1950s it became obvious that the main-frame computer would find application in the research laboratory. Since then, the systems analysts, often not chemists themselves, have extended classical computer science to the correlation of data in quality control, process control and the analytical laboratory.

In the next decade the minicomputer emerged as a tool in laboratory automation. It combined some of the abilities of the large computer with the control operations so necessary for automatic data acquisition.

In the 1970s microprocessors and microcomputers came to the forefront. These large-scale integrated-circuit devices offer very inexpensive means of control and data acquisition, encouraging instrument designers to incorporate them in laboratory equipment. Thus we now have the so-called 'intelligent' instrument, capable of autocalibration, data collection, transmission, processing and display, and even diagnosis of any faults developed.

In many laboratories, several instruments are linked to a central minicomputer, giving a self-contained multichannel automated unit.

For example, Overton *et al.* [152] described a system in which eight instruments, comprising gas-liquid chromatographs, automatic analysers and pulse polarographs, were sampled at different data rates by a computer which also processed the stored data.

De Voe *et al.* [153] used a multiprogrammed minicomputer in a system supporting twenty instruments comprising spectrophotometers, electrochemical cells, a mass spectrometer, electron-probe microanalysers, gamma-ray spectrometers, Mossbauer spectrometers and an electron spectrometer, for chemical analysis.

It is probably operationally more efficient if instruments with fast data-collecting rates (such as mass and NMR spectrometers) have their own (dedicated) computers whereas those with slow data-collecting rates (such as infrared and ultraviolet spectrophotometers, microcalorimeters and gas chromatographs) share a common central computer.

Dessy and Titus [154] have described design considerations for interfacing analytical instrumentation with computers. Computer interfacing to chemical instruments, and the processing of the resulting data, have been discussed under the headings of data acquisition and analogue-to-digital conversion; digital preprocessing; procedural reduction; manipulation and transformation; and postoperative amalgamation and interpretation [155].

We have mentioned above that present laboratory apparatus with an advanced degree of automation, is equipped with microprocessors. Some useful indications of trends will be found in a special issue of *Talanta* [156].

In order to understand the modes in which the microprocessor may operate, it is useful to look carefully at how different types of computers interact with data sources and human operators.

At first, digital computers were used by scientists in an 'off-line' mode [157], in which the data were collected, fed to the computer together with the program, and processed. If a central computer was used, the processing had to wait until computer time was available. Even with a computer dedicated to the experiment, the scientist had to collect the data and transfer them to the computer input.

The advent of the moderately priced minicomputer not only brought the processing into the laboratory but through direct input of data through a microprocessor was able to give on-line processing [157].

The experimentalist then interacts with the minicomputer, which in turn obtains the data, makes decisions, calculates variables and returns the results actually during the experiment ('real-time' processing). In this mode, the computer remains a distinct entity, designed as a general-purpose machine, but is used for one particular purpose.

The microcomputer, originally designed to replace hard-wired logic circuits in dedicated machines and instrumentation, also gives real-time processing.

Microprocessors are now incorporated into a wide range of analytical instruments. This application might be termed 'in-line', since, to the operator, the computer and the instrument are virtually one unit [157].

The operator communicates with the computer and directs its operations but does not program it; the program is built in (as a permanent memory) by the maker. Thus the instrument does not appear to the operator to be a computer: it is simply a more powerful (even 'intelligent') instrument.

Trends and developments in computer-controlled equipment and laboratory automation have been reviewed by Stockwell [55] and by Perrin [158] some examples are given in Table 2.15.

From this table, it may be observed that a great many current high-performance laboratory instruments are controlled by computers. The operational parameters of such instruments are sensibly improved, the analytical information being thus obtained at any time in direct form. It will be sufficient to give a simple example regarding the performance of the system GC/MS/computers.

Although any two of these techniques are often combined, a remarkable

synergism occurs when all three are integrated into a single unit. An unusual analytical performance emerges [159]. The use of such instruments can indeed give us almost incredible results. This is the case for the Hewlett-Packard series 5980 A GC-MS equipment. The 5933 A Data System employs an HP 2100 S minicomputer with 16 K of core memory, completely programmed for on-line control of the mass spectrometer as well as automatic data reduction. It has a dual disc-drive system for input/output and storage, and a paper tape reader for

Table 2.15

Examples of computer or microprocessor-controlled apparatus

- Atomic-absorption spectrometers
- Atomic-fluorescence spectrometers
- Automatic titrators
- Automatic titrators with ion-selective electrodes
- D.C. arc spectrometers
- Electron microprobes
- Electron spin resonance spectrometers
- Flame emission spectrometers
- Flow-injection analysers
- Fourier-transform infrared spectrometers
- Gamma-spectrometers
- Gas chromatographs
- Gas-chromatograph/mass spectrometer systems
- Gradient HPLC
- Luminescence spectrometers
- Mass spectrometer detectors for liquid chromatography
- Microwave spectrometers
- Nuclear magnetic resonance spectrometers
- Particle size analysers
- Plasma emission spectrometers
- Polarographs
- Potentiometric analysers
- Raman spectrometers
- Spark-source mass spectrometers
- Spectrofluorimeters
- Surface area analysers
- Thermal analysers
- Ultraviolet-visible region spectrometers



updating with new programs. Each disc can store over 12000 mass spectra per GC run, typically over 10 hours of uninterrupted analysis. It is easily expanded to 255 interchangeable catalogued discs providing over  $5 \times 10^9$  bits of memory [160].

## CHAPTER 3

# Education in Analytical Chemistry

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Before we discuss this problem, we should try to define analytical chemistry. A broad working definition might be that it is the application of physical chemical principles and inorganic and organic reaction chemistry to inorganic and organic materials for determination of their composition, structure and identity. The subject therefore has exceedingly wide scope. However, it goes rather deeper than this definition suggests. In particular, it is essentially concerned with the solution of the problems posed by the demand of science and technology for accurate information, and thus requires analysis of each situation as it arises. Analysis is defined as the process of determining composition etc., or the report of the composition thus found, and also as *tracing of things to their source*. It is this last part of the definition that is the key to education in analytical chemistry. The true analyst is not content with being able to perform an analysis correctly, he also wants to know how and why the system works, so that he can apply it intelligently and correctly. This is the basis of Lundell's famous distinction between 'determinators' and 'analysts' in his article 'The Chemical Analysis of Things as They Are' [161], which is as valid today as it was when written nearly 50 years ago.

Once we have decided what we mean by analytical chemistry, we can decide which aspects of it we believe are essential knowledge for an 'educated' analyst, and then about the best way to ensure that the knowledge is really understood and correctly applied; in other words, to ensure that the analyst really has become educated. To our way of thinking, the only sure means of doing this is by analysis itself, namely by problem solving. It is a common experience amongst university teachers that students who revise their work only by reading their lecture notes, frequently mistake recognition for knowledge and understanding. It is only by trying to apply their learning by solving problems (or explaining things to others, which is what happens in examinations) that they can discover whether they *really* know something or only *think* they know it.

We shall therefore set out our choice of illustrative material in the order in which the educated analyst performs the various steps in an analysis. To put

the material in 'modern' terms, we shall use the terminology of automation. Our choice of material is subjective in some respects, and others will have their own favourite themes and illustrations, but that does not affect the principle or alter the logic of our argument.

### 3.1 INPUT

#### 3.1.1 Definition of the Problem

Just as a doctor needs to take a case history before he can decide what treatment the patient needs, the analyst must obtain enough information about the analytical problem for him to be able to decide on the best technique to use (or even whether he is being asked a sensible question in the first place). The series of articles 'The Analytical Approach' appearing from time to time in *Analytical Chemistry* can serve as a good illustration of the need for a case history. The story of the organic sample that gave zero carbon content on combustion analysis is a good example of a 'nonsense' question (the compound was a fully halogenated hydrocarbon, developed as a flame-retardant).

Once the problem has been defined, the problem of sampling can be dealt with, followed by choice of method, interpretation of results, and reporting.

#### 3.1.2 The Sample

An analysis cannot be better than the sample.

The Analytical Commission of Terminology of the International Union of Pure and Applied Chemistry defines the sample as 'a portion of material taken from the consignment and selected in such a way that it possesses the essential characteristics of the bulk'.

If the chemical analysis is to give meaningful results, some important rules must be observed when the sample is taken. First, it must be representative, i.e. of the same composition as the material from which it originates. This requirement is relatively easy to fulfil when homogeneous materials (gases, liquids) are sampled, but sampling of a large bulk of solid heterogeneous material is a very difficult operation.

Secondly, it is very important for the analyst to decide the amount of sample that has to be analysed. This amount depends on many factors, such as the mass available for testing, its state and composition (dimensions, shape, uniformity of distribution and specific mass of granules), the proportion of component to be determined; the size of the glassware used, the sensitivity of the methods employed, the accuracy required, the cost of the sample, etc.

Thirdly, the sample must be handled and stored with special care to avoid changes in composition (losses of fine particles, loss or absorption of moisture, alteration in contact with air or on exposure to light, contamination by container wall corrosion, loss by adsorption on container walls, etc.).

If these rules are not kept the sample may not be a reliable representative of the whole, and the analysis will be more or less worthless.

### 3.1.3 Sampling

The overall analytical process of determining one or more of the components of a sample consists of six operational steps which are carried out in a certain sequence, as shown in Fig. 3.1, where it is seen that definition of the purpose of the analysis is followed by selection of the sample on which the work is to be performed. Sampling is a complex topic only partly amenable to theoretical description.

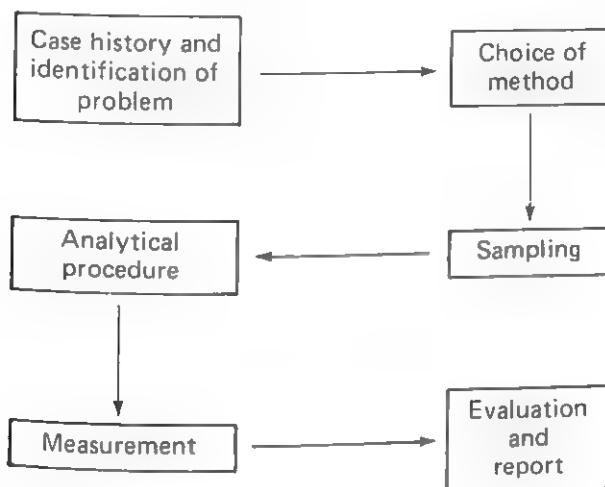


Fig. 3.1 – The analytical process.

Sampling is an operation of outstanding importance and if it is not properly done, the operations that follow (decomposition, separation, conversion of the constituent into measurable form, measurement and interpretation of data), even though performed correctly in themselves, will give incorrect results.

Young chemists do not realize the attention that must be given to sampling; they may realize it, however, when they face the problem of sampling from 10–500,000 tons of material or more, in a truck, railroad wagon, a mineral shipment, or a mineral deposit, the material itself consisting of a heterogeneous mixture of fine particles, granules and lumps which may be up to a metre or more across.

The analyst may receive the sample as such and not participate in the sampling or may supervise all the operations of sampling and preparation of the sample for analysis. In the first case, analysts who are idle will confine themselves

to performing the analyses without assuming any responsibility regarding sampling, packing of samples and their transport to the laboratory, and in Lundell's terminology [161] are only 'determinators'.

Such reliance on others can lead to bizarre results, such as the packing material being sampled instead of the contents of the package (though in this case the error was quickly discovered). If they are well trained and highly dependable, however, they will want to know the whole history of the sample (the way it was taken, reduced, crushed, packed and transported) since only on the basis of this knowledge can they decide whether the sample will be satisfactory for the purpose of the analysis to be fulfilled or must be replaced by another one. The wise analyst, of course, will whenever possible supervise all stages of sampling and preparation of samples for analysis, so that he can take full responsibility for the results.

In order for the analytical process to be ensured favourable conditions and for the results to justify the work, the analyst has to recognize the importance of correct sampling and be well acquainted with the statistical background of sampling, the general methods of sampling various types of materials, the proper transmission and storage of samples, the pitfalls that may lead to bias in sampling, the use that is to be made of the analyses, etc.

Any additional information, such as the purpose of testing, specification limits for a constituent of a sample, or the desired accuracy of analysis must not be regarded as superfluous, and background knowledge is often necessary. For example, when a component of a deposit of useful minerals has to be evaluated, a knowledge of geology, geochemistry and mineralogy is needed since it facilitates the drawing of conclusions on the distribution of the constituent vertically or horizontally within the deposit.

Although the methods and techniques of separation and measurement have developed spectacularly, the methods and techniques of sampling have not enjoyed the same attention. Sampling is habitually done manually and mechanical tools are employed only to a small extent. However, in some isolated cases special sampling techniques have been developed, such as the devices for sampling the ocean bottom or the high atmosphere, or which pick up samples of equal volume at equal time intervals and are used in automatic and on-line analysis.

A very important problem in testing for a constituent of a material is to know how it is distributed in the bulk material. If the distribution is normal, the content of the constituent may be obtained from a small number of analyses and the application of statistics.

Statistical sampling is based on the principle that all particles or portions of the material (the population) have an equal probability of being present in the sample. Thus a sample is a portion of the population taken in such a manner that it is representative of that population. The parameter (e.g. the content of one constituent) which is determined in the analysis is assumed also to have a normal population distribution. If an infinite number of measurements of the parameter

could be made and the frequency of occurrence of given values plotted against the values, a symmetrical peak would be obtained (Fig. 3.2) described by the well-known equation:

$$y = \frac{1}{\sigma\sqrt{2\pi}} \exp\left[-\frac{(x-\mu)^2}{2\sigma^2}\right] \quad (3.1)$$

where  $y$  is the variance of the population, equal to the average of the squares of the deviations from the mean;  $\sigma$  is the standard deviation of the population, equal to the square root of the variance;  $\mu$  is the average value of the parameter measured (arithmetic mean);  $x$  is an individual value of the parameter.

Figure 3.2 shows that almost all the values of the parameter (99.74%) lie within the interval  $\mu \pm 3\sigma$ .

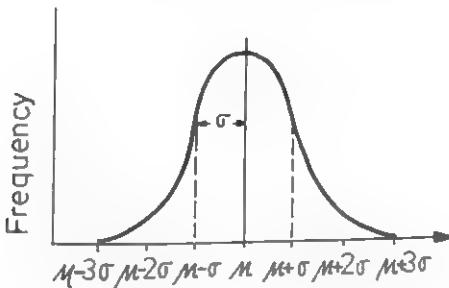


Fig. 3.2 – The normal distribution law.

There are populations of interest for the analyst which do not follow a normal distribution, and require special statistical treatment which is beyond the aim of this chapter (it may be found in texts on statistics applied to analysis, e.g. [85, 150, 162, 163]).

In practice, of course, the individual members of the population generally *do not* have an equal probability of being present in the sample taken for analysis, because the sample will never consist of a single completely uniform species, unless it happens to be a single elementary particle (which is a *reductio ad absurdum*). Hence there will always be an inherent variance (the sampling error) in the composition of the sample withdrawn and analysed. In addition to this there will be the variance of the analytical results, caused by the random errors in the analysis itself (analysis error). The overall error will then be described by the rule that the variance of a sum or difference is the sum of the individual variances. If one of the individual variances is more than about ten times the other, the smaller variance will contribute little to the overall variance and for practical purposes can be ignored.

The question then arises of how many analyses must be performed on a given

population for the overall error to lie within some preset limits. Analyses are expensive and labour-intensive, so both the customer and the analyst will want the number to be the minimum needed to ensure the desired accuracy. Suppose we choose an 'acceptable' absolute error  $\Delta_{\max} = |x - \mu|$  and a certain probability that it will not be exceeded. From tables for the Gaussian distribution we can find the value of  $z$  which gives the desired probability that the absolute error of the result will not exceed  $|z \sigma|$ , where  $\sigma$  is the standard deviation. We then use the relationship

$$z = \frac{\Delta_{\max} \sqrt{n}}{\sigma} \quad (3.2)$$

to calculate the number of determinations needed ( $n$ ). If  $\sigma$  is not known and has to be replaced by its estimate,  $s$ , obtained from a small number of replicate measurements, then instead of  $z$  we use the corresponding value of  $t$ , found in tables of the 'Student-*t*' distribution [164].

An alternative which makes no *a priori* stipulations is to use the equation

$$\Delta = ts/\sqrt{n} \quad (3.3)$$

in an examination of the effect of  $n$  on the magnitude of the absolute error  $\Delta$  [165]. We can then easily see whether increasing the value of  $n$  above a certain number will reduce  $\Delta$  significantly or not. Take for example the case of determination of 10% of component X, given that the standard deviation (determined by analysis of a pure compound) is 0.10% at this level. For a probability of 0.95 that the experimental error will not exceed  $|t s|$ , we find that  $\Delta$  is 0.90 for  $n = 2$ , 0.25 for  $n = 3$ , 0.16 for  $n = 4$ , 0.12 for  $n = 5$ . In terms of cost-effectiveness it is worth doing three analyses, but probably not four and certainly not five.

We can extend the treatment to include the sampling error as well as the analysis error, and can either calculate the number of analyses needed to give a reliable mean value for a given value of sampling error, or estimate the magnitude of the sampling error from the results of a given number of analyses. If we use  $s_t$ ,  $s_s$ , and  $s_a$  to signify the total, sampling, and analysis standard deviations respectively, we shall have

$$n = t^2 s_t^2 / \Delta^2 \quad (3.4)$$

and

$$s_s^2 = \frac{n \Delta^2}{t^2} - s_a^2 \quad (3.5)$$

In these cases it is necessary to have at least a rough idea of the relative importance of  $s_s$  and  $s_a$ . Suppose these quantities have the values 1 and 0.2 respectively. Then the value of  $s_t$  will be 1.02, practically the same as that for  $s_s$ , and the number of samples needed is then  $n = t^2 s_s^2 / \Delta^2$  and each sample need be analysed only once.

On the other hand, if  $s_a$  is appreciably greater than  $s_e$ , unless a better method of analysis can be found it will be necessary to analyse each sample a sufficient number of times to reduce the analytical variance sufficiently for it not to affect the total variance significantly, and to take the requisite number of samples to achieve the desired value of  $\Delta$ . Proper design of a sampling pattern (and proper choice of analytical method) is clearly important in terms of time and economics. For on-line control or for control-chart purposes, the frequency of sampling, cost of analysis and cost of 'off-specification' production must be taken into account in deciding. Such considerations are discussed by Davies [166] and by Kortlandt and Zwart [167] amongst others.

Sometimes sampling will be affected by accidental mistakes. The statistical approach to sampling is based on the assumption that all particles or portions of the population are equally likely to be present in a sample picked out at random. However, in practice, the amounts of sample taken from the surface (or periphery) and the interior of the material will vary and so the sampling will not be truly random. Again, the sample picked out may contain a non-representative amount of coarser or finer grained material. All these are mistakes that affect the selection of representative samples. As an illustration we may mention the problem of testing for heavy titanium and zirconium ores in an alluvial material. Transverse lines were set on the river bed and holes were dug into the sand at certain spacings, down to the water-bearing layer. Primary samples of 10 kg each were taken from the holes at a preselected depth. After manual removal of rough material, the samples were 'panned' (i.e. washed by stirring and decantation) until a few tens of grams of heavy mineral were left, which after drying and weighing were examined under the microscope. It is noteworthy that there was no agreement between the weights of heavy mineral samples from the same depth in neighbouring holes. Owing to this lack of agreement the operation was carefully examined; it turned out that some workers selected more coarse material from the primary sample while others chose more fine material; some washed samples more carefully, some less carefully. A significant improvement was achieved by placing a bucket in the hole to give direct and more random drawing of the primary sample; the panning was continued until there was complete removal of light-coloured particles (quartz, mica, etc.).

### 3.1.3.1 Sampling of Gases

The properties of gases, their dependence on temperature and pressure, stratification according to density, and the difficulties associated with storage and transport all indicate that gas samples should be analysed immediately after they have been taken.

Samples of gas are drawn by aspiration, displacement of liquids or expansion into evacuated receivers. The devices for gas sampling are generally cylindrical, made of glass and provided with suitable taps. Metal taps that do not need greasing to ensure gas-tightness are recommended.

Gas samples are generally collected over mercury, water or salt solutions so that the volume and pressure can be controlled, provided that none of the components is absorbed by or reacts with the liquid used.

The method of sampling depends on the nature of the gaseous material. For example, the method of aspiration through successive cylindrical vessels ensures a representative sample of a mixture of gases in one of the first vessels after the taps have been turned off, but this method could not be applied for obtaining a representative sample of a mixture of liquid gases having different boiling points.

An important and difficult problem is the sampling of atmospheric air. There are factors such as wind, precipitation, convection currents, pollution intensified by human activity, etc., that modify the local composition of the atmosphere, especially with respect to the minor components. The atmosphere contains numerous noxious solid, liquid and gaseous substances, radioactive isotopes, bacteria, etc., introduced by pollution, which endanger public health; therefore the composition of the atmosphere has to be analysed ever more frequently. Because of the continuous change in atmospheric composition, taking a representative sample of the whole is pointless as well as impossible; the only useful approach is to analyse samples taken at many places at short time-intervals.

Only small amounts of the noxious substances are present in the atmosphere so if small sample volumes are drawn the danger exists that the substance sought will be present at below the detection limit of even the most sensitive methods. Therefore relatively large volumes of air are sampled by means of flow-meters provided with filters which retain the solid particles, with membranes to retain aerosols [168], and various solutions to absorb the gaseous components differentially.

The need to analyse large numbers of air samples has led to the development of automatic methods of sampling and determination of microcomponents.

### 3.1.3.2 Sampling of Liquids

Liquids are sampled by flow, pipetting or siphoning.

If the liquid is not stratified by immiscibility or differences of density, it can be homogenized by shaking before the sampling.

Liquids with immiscible layers are sampled by pipetting from each layer a volume proportional to the layer thickness; the layer samples are analysed separately or recombined to give a representative sample.

When the liquid contains suspended solids their dissolution by stirring or heating must be attempted. If dissolution is not possible the suspension is filtered and the two phases analysed separately.

A liquid with components of somewhat different volatility is sampled in two vessels connected in series. The liquid flows into the bottom of the first vessel through a tube fitted with a tap and when the vessel is full flows through

an overflow into the bottom of the second vessel. Flow is continued until a representative sample is ensured in the first vessel.

Special attention must be paid to sampling of liquids when the aim is determination of the gas content of the liquid. For example, a water sample for oxygen determination must be drawn and handled so that there is no exposure to the atmosphere. The sample is then brought to boiling at a pressure so low that the amount of oxygen dissolved is practically zero. The gases evolved are collected over mercury in a graduated test-tube and an oxygen-absorbing solution is added. The decrease in gas volume gives the oxygen content of the sample. Details of water sampling for oxygen determination are given by Buchoff *et al.* [169].

Another important problem is sampling and analysis of large volumes of flowing (springs, rivers, industrial effluent) or standing (lakes, seas, oceans) waters. The chemical composition of a flowing water changes with precipitation, temperature, flow-rate, distance from source, depth, pollution, sources, etc. Likewise the composition of water in lakes, seas, oceans changes with depth, temperature, streams, existence of sources of feed or pollution, etc. For example, the free oxygen content of water changes with diurnal temperature, season, geographical location (mountains or plains), depth, etc. Sampling at different depths is achieved with special devices that open and close when a certain depth is reached; these devices are called bathometers. On account of the large number of factors that affect the composition of waters, representative samples cannot be drawn from large volumes of water and a large amount of information may be obtained only by performing a very large number of analyses.

The demand for large numbers of analyses of liquids (natural waters, waste waters, production streams, blood, etc.) has necessitated automation of many methods of analysis. This in turn has entailed development of adequate methods of automatic sampling of volumes ranging from a few  $\mu\text{l}$  (blood samples) to several ml. A blood sample may be taken from the drop obtained by pricking the fingertip. Constant-volume liquid samples for continuous flow analysis may be drawn by the special device developed by Jansen *et al.* [170]. The volume of sample fed to the analyser is that enclosed between two air-bubbles. Two platinum-tube electrodes are placed in the analyser feed-tube and remain in electrical contact as long as conducting liquid flows between them, but passage of an air-bubble breaks the contact. The sequence of events is shown in Fig. 3.3; the inlet of the feed-tube is open to atmosphere during successive movements of the turn-table holding the sample-tubes, and an air-bubble is thereby introduced, followed by the liquid drawn in from the next sample-tube until the air-bubble reaches the electrodes and contact is broken. When the air-bubble has passed through the electrode pair the current is restored and this actuates the next movement of the turn-table, causing the next air-bubble to be drawn in. The plug of sample between the two air-bubbles then passes into the analyser. The actual volume taken need not be known (since standards are sampled in the same way).

and the amount of sample can be optimized with respect to the analytical method by using feed-tubes with different internal diameters.

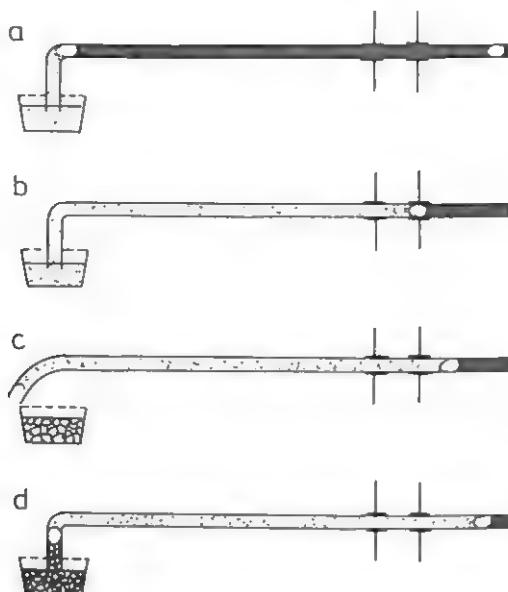


Fig. 3.3 – Constant volume sampling technique for continuous flow analysis.  
a, sample is taken, samples separated by an air bubble; b, air bubble passes second electrode, initiating rotation of sample plate; c, another air bubble is aspirated; d, new sample is taken [170] (by permission of the copyright holders, Elsevier North-Holland Biomedical Press, Amsterdam).

### 3.1.3.3 Sampling of Solids

Unlike the sampling of gaseous and liquid materials, in the case of solids an additional factor appears: the particle size. Most solid materials consist of particles of various sizes, and are characterized by pronounced heterogeneity. Moreover, the species of interest may be present only in a particular type of particle (fine, coarse, or discrete pure particles) or generally in particles throughout the material. The various fine particles, granules or lumps present also take many different shapes. All these features increase the difficulty of representative sampling of solid materials.

#### *The weight of sample*

It is very important to know the amount of sample to take. It varies, depending on the purpose, within very wide limits, from several tons (for technological testing) to several grams (for chemical analysis).

If the solid material were made up of equally sized particles with the constituent of interest uniformly distributed in them, the precision of sampling should be independent of the size of samples, as in the case of fluids. However,

the minimum amount of sample to be taken from solid materials depends on the size, number and shape of the granules, the average content of the species to be determined, the difference between the specific gravities of the components, and the magnitude of the acceptable error.

To determine the amount of sample, several empirical equations are employed, which take into account the particle size and the nature of the material.

Thus Bailey [171] suggested that the size/weight ratio should be taken as a criterion of sample size:

$$b = \frac{\text{wt. of largest particle} \times 100}{\text{wt. of sample}} \quad (3.6)$$

The value of  $b$  that would give results agreeing within the acceptable experimental error was determined experimentally by work with various types of coal. It was also determined from the equation  $s = \sqrt{bp}$  where  $s$  is the standard deviation (of the content of a given species) due to sampling and  $p$  is the content in question. When this was applied to a limonite ore on the assumptions that limonite contains about 10% silica, that all of the silica is present as the largest particles (assumed to be cubic and having a density of  $2.6 \text{ g/cm}^3$ ), and that the sampling standard deviation of the silica content shall not exceed 0.05%, it was concluded that a sample of 39.4 kg would be required when the component particles had a side of 0.336 cm, but only 1 g when the particle side was 0.0046 cm [172].

Ceciott, quoted by Demetrescu *et al.* [173] advanced an equation which is widely used in practice:

$$q = kd^2 \quad (3.7)$$

where  $q$  is the weight of ore sample (kg),  $d$  the particle diameter (mm) and  $k$  a coefficient which depends on the properties of the ore.

Table 3.1 gives the values of  $k$  for different types of ores.

Table 3.2 was derived from values calculated by Ceciott's equation; it shows the influence of the type of ore and of particle size on the amount of sample.

Harris and Kratochvil [174] have given a statistical interpretation of relationships between the sampling error, size of sample, number, dimensions and density of particles, and the amount of constituent of interest. They made several simplifying assumptions. The material to be analysed was considered to consist of two types of particles of the same size and of uniform density. Type A contained the constituent of interest, and type B did not. The distribution of types A and B was assumed to be random and the composition of the two types uniform. The relative standard deviation ( $\sigma, \%$ ) for component A was then taken as given by the Bernoulli equation:

$$\sigma_s = 100 \sqrt{(1-p)/np} \quad (3.8)$$

Table 3.1  
The values of coefficient  $k$  for different types of ores [173]

Ore	$k$
Coal	0.3-0.5
Homogeneous ferrous ores	0.02-0.3
Inhomogeneous ferrous ores	0.5-2.0
Non-ferrous disseminated ores	0.2-1.0
Complex sulphides of non-ferrous metals with uniform distribution of the useful ores	0.4-0.5
Rare metal ores (W, etc.)	0.2-2.0
Auriferous quartz	1.0-3.0
Homogeneous apatite ore	0.4-0.15
Ceramic feldspath	0.2-4.0

Table 3.2  
The size of samples as a function of ore type and particle size [173]

The amount of sample $kg$	The diameter of large particles, mm				
	Very poor or very uniform ores	Poor or uniform ores	Middle ores	Rich or non-uniform ores	Very rich or very non-uniform ores
10 000	207	114	76	32	5.5
5000	147	80	54	22	3.8
2500	107	57	38	16	2.7
1000	65	36	24	10	1.7
500	46	25	17	7	1.2
250	33	18	12	5	0.9
100	21	12	8	3	0.5
50	15	8	5	2	0.4
25	11	6	4	1.5	0.3
10	7	4	3	1.0	0.2
5	5	3	2	0.7	0.1
2	3	2	1.2	0.5	-
1	2	1	0.7	0.3	-
0.500	1.5	0.8	0.5	0.2	-
0.250	1.0	0.6	0.4	0.1	-
0.100	0.7	0.4	0.3	-	-
0.050	0.5	0.3	0.2	-	-
0.025	0.3	0.2	0.1	-	-
0.010	0.2	0.1	-	-	-

where  $n$  is the number of particles,  $p$  is the fraction of the component A and  $(1 - p)$  the fraction of diluent B. For the case that the A-type particles are 100% pure component of interest, the dependence of  $\sigma$  on  $p$  (for  $p$  between 0.0001 and 0.999) and on  $n$  is shown in Fig. 3.4. If  $\sigma$  is taken as a measure of the sampling error, which is really related to the homogeneity of the sample, Fig. 3.4 shows that if A represents a trace constituent (i.e.  $p$  is very small), a very large number of particles must be taken if the error is to be kept small.

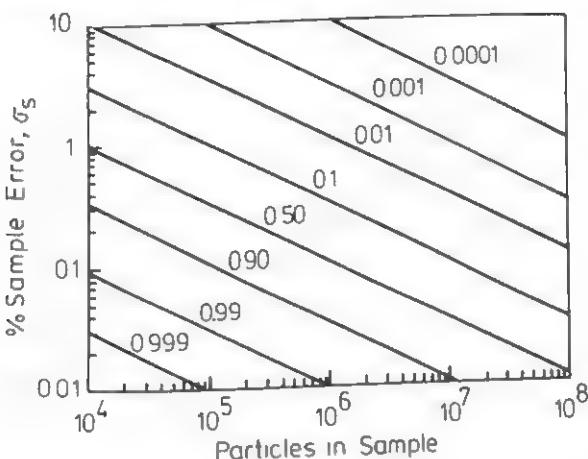


Fig. 3.4 – Relation between the sampling error  $\sigma_s$  in percentage and the total number of particles  $n$  for samples in which  $p$  ranges from 0.0001 to 0.999 [174]. (Reprinted with permission from *Anal. Chem.*, 1974, **46**, 313. Copyright by the American Chemical Society.)

A correlation between particle size and the number of particles per gram of sample, for particles of a given density, is shown in Fig. 3.5. It is seen from these two figures that for the sampling error to be 0.1% for a determination of 50%

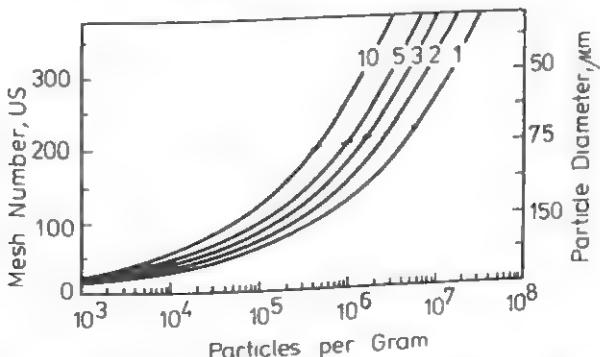


Fig. 3.5 Approximate relation between the number of spherical particles per gram of sample and mesh size (U.S. Sieve Series, ASTM E-11-61) or particle diameter, for densities from 1 to 10 [174]. (Reprinted with permission from *Anal. Chem.*, 1974, **46**, 313. Copyright by the American Chemical Society.)

silica in a rock sample of density 3 g/cm<sup>3</sup>, the analyst would require at least 10<sup>6</sup> particles in the sample, and thus would need to grind the material to pass a 170-mesh sieve (U.S. or British Standard), if a 1-g sample were used.

Many attempts have been made to arrive at a statistical theory of sampling error. It is easy to establish equations for the idealized case of a two component mixture of particles of identical size and shape, the species of interest being present at a different level in the one component from that in the other, but uniformly distributed in a particular component. This was first done by Baule and Benedetti-Pichler [175] on the basis of the Bernouilli equation, and has been extended by Wilson [176] and by Ingamells and Switzer [177,178]. Real systems are often far from ideal, of course, and in any case there are additional problems not allowed for in the idealized systems. In trace analysis, for example, if the element of interest is a trace constituent in one or more of the major types of component and is not a major constituent of a minor or trace component, the error caused by inhomogeneity in the sample taken for analysis will be small, whereas for the reverse case of the trace element being concentrated in a minor component of the mixture, the sampling error due to inhomogeneity will be large and a very large sample will be needed [179,180]. The classical example is gold particles in sands.

The theory has also been extended to cover particle size distribution and the concentration distribution between different components of the mixture [181] and the results clearly show that the largest particles have the greatest influence on the inhomogeneity of the sample (which is why prudent housewives always cut a large potato in two *before* peeling it, to save effort if it is rotten inside).

If the particle sizes and densities of the components are very different, then segregation can very easily occur, as can readily be demonstrated to students with a mixture of salt, sugar and sand. It is always necessary to comminute the material sufficiently for the sample taken to contain an adequate number of particles of each constituent. Segregation has been considered by Visman *et al.* [182-184].

The problem of sampling particulate solid material has been reviewed by Gy [179] and by Grant and Pelton [180].

In general, the sample weight is not determined solely by statistical considerations of the kind just discussed, but may also depend on the nature of the species to be determined, and the performance characteristics of the analytical method used. Most destructive methods of analysis use samples in the weight range between about 5 mg and 1 g, but for determination of gold (a malleable and ductile element, occurring as the free element), much larger samples (e.g., the 'assay ton', approximately 29 g) are required.

Non-destructive methods (X-ray fluorescence, microprobe, etc.) by their very nature usually require small samples, but because one of their main purposes is identification and analysis of inhomogeneities, also require repetitive application and averaging, preferably with scanning over a reasonably large area.

### *Methods of sampling*

It is impossible to establish a method of sampling that applies to all solid materials; all that can be said is that sampling must always be conducted with special care and conscientiousness, especially as manual sampling is the most common method.

Sampling of stationary materials (ore deposits, waste dumps, silos, ores in trucks and in coffer dams, etc.) is performed according to agreed rules. A large amount of sample is taken, made up of partial samples taken from imaginary sections marked on the material. Material being transported is sampled during loading or unloading.

The main method of sampling materials in motion (on conveyor belts) consists of manually or mechanically taking out certain sections of material; this can be done along or across the material, continuously or at equal time intervals. The portions sampled are combined to give the representative sample.

Process-control in industrial plant is achieved with samples taken from any point of the line, according to the technology and the purpose of the analysis. If there is closed-loop control of the process (p. 69), it is essential to take the sample as close to the process or reactor as possible, and to place the analyser very close to the sampling point.

### *Obtaining samples for the laboratory*

Sampling produces large amounts of material consisting of granules with dimensions not suitable for subsequent testing. Therefore, these samples are crushed, homogenized and reduced until they have suitable weight and particle size.

Crushing is done mechanically or manually, depending on the mass of sample and the dimensions and hardness of the components. Crushers, roller etc. are used for crushing; each is employed in turn to reduce the particle size to the required fineness.

Samples are homogenized manually or more often mechanically by ball mill. Homogenization is followed by reduction of sample size either by quartering or in the divider method. Quartering consists of gathering the homogenized material in a conical heap, dividing it into four quarters, retaining two opposite quarters and throwing the other two away. The material retained is quartered repeatedly in the same way until the required amount of sample is obtained. The sample may equally well be arranged in two rows of squares (20-30 in all), every second square being retained and the others disposed of, the operation then being repeated.

Quartering is slow and laborious, and requires a great deal of space. These drawbacks are very evident when say 50 tons of material must be sampled to produce an analysis sample of only several grams or tens of grams.

The divider method is an improvement on quartering. The device used consists of an even number of grooves positioned so that neighbouring grooves empty their content on opposite sides, into two receptacles. The material collected in one receptacle is used for further similar operations, continued as long as necessary, with dividers with increasingly narrower grooves.

#### *Preparation of samples for chemical analysis*

Solid samples such as ores or rocks received in the laboratory for analysis usually have a grain size of about 1 mm and weigh between 0.2 and 2 kg. They must be further reduced (by quartering) to a mass of several grams, then crushed in a mortar until the particles are less than 0.060 mm in diameter (pass through the  $10^4$  mesh/cm<sup>2</sup> sieve). Then the samples are either stored in screw-cap bottles ('as received' samples) or dried in the oven at 105–110°C for 1–2 hours and then stored in a desiccator.

#### *3.1.3.4 The Dispatch and Conservation of Samples*

Samples are sent to laboratories for analysis according to rules which ensure preservation of their integrity and identification.

Depending on their nature and consistency, samples are transported in airtight metal, glass or plastic containers, plastic or waxed paper bags, etc. It is very important that samples are protected against contamination during handling, transport and storage. Some samples may change in composition if exposed to moisture, carbon dioxide or oxygen, or may decompose in presence of light or as a result of temperature changes. A frequent source of contamination is reaction of the sample with the container material. To avoid this, it is necessary to choose the container according to the properties of the sample (volatility, corrosivity, dissolving action) and the constituent sought. For example, a water sample to be analysed for boron must be taken and transported in soda glass and not borosilicate glass. Alkaline samples must not be stored in glass vessels. Samples for trace-element determination have to be stored in plastic containers, but these are not suitable for organic solvents. Some constituents of samples can be preserved only by fixing, i.e. conversion into a more stable state. Thus in water samples, hydrogen sulphide is fixed by precipitation with cadmium, zinc or copper salts; oxygen is fixed by precipitation with manganese(II) salts; hydrogen cyanide is fixed by addition of sodium hydroxide.

Fortunately, most solid natural samples are very stable. Thus samples of ore and rocks may be packed in coated paper, plastic sheet or wooden crates for transport and storage. However, careless handling during transport may result in loss of fine particles, and the sample is no longer representative when it reaches the laboratory. Such negligence may have the most surprising effects. For example, an on-site examination of 10-kg samples of an alluvial deposit showed that the fine particles contained titanium and zirconium minerals [185] but when several tons of the deposit were sent to a central laboratory and attempts were

made to separate the titanium and zirconium minerals, much to general surprise none were found. Investigation showed that owing to negligence during transport, the fine material containing titanium and zirconium had been lost and only the coarse material had reached the laboratory.

For identification, the package must be clearly labelled with the source, the number of the sample, details of the sampling, name of the sampler, and the components to be determined.

After the analysis has been done and the report made, the sample should be stored for some time, in case dispute arises.

### 3.1.4 Decomposition of Samples

The samples to be analysed are usually gaseous, liquid or solid mixtures, though sometimes they may consist of two or even all three states of matter, and for most methods of analysis, except a few non-destructive physical methods, must be converted into a one-phase system with the components of interest in measurable form. Hence, solid samples have to be brought into solution.

The solubility of a substance is determined by the forces of attraction between its fundamental particles (ions, molecules) and between those of the solvent, and those between the solute and solvent (solvation forces). In general the solvation forces are related to similarity of structure of the solute and solvent. That is, a substance dissolves preferentially in a solvent with a structure similar to its own, an example being the high solubility of lower alcohols in water and of higher alcohols in organic solvents.

Dissolution of a substance is accompanied by the evolution or absorption of an amount of energy referred to as the heat of dissolution, which is the difference between two thermal effects: the energy required to detach ions or molecules from the solid material lattice and provide them with kinetic energy of translation in solution (and to make holes in the solvent structure to accommodate them), and the energy released by solvation of the ion or molecule (solvation is the formation of a layer of solvent molecules around the molecule or ion dissolved). One of the two effects (the binding energy of the solid or the solvation energy) prevails and the solvation process is accordingly endothermic or exothermic. The dissolution process takes place at the interface of the two phases, so the sample is finely crushed to increase the surface area exposed, and the system is heated to increase the rate of the process.

The solvents are selected according to the composition and structure of the materials to be dissolved, care being taken to see that the excess of solvent does not affect the further steps in the analysis. Many synthetic or natural materials such as some metals, minerals, ores and rocks are difficult to dissolve, and special techniques are sometimes required.

Although the common techniques of dissolution have been known for a long time, even in this field some progress has been achieved, in particular in development of reagents, chemically and thermally resistant reaction vessels, methods of

attack, control of contamination, and evaluation of dissolution efficiency [186]. The books by Šulcек *et al.* [187] and Bock [188] are invaluable aids in choosing decomposition methods.

### 3.1.4.1 Dissolution

Strong acids, alone or in mixtures, dissolve many solid substances. Salts of weak acids dissolve in so-called non-oxidizing strong acids† by simple protonation of the anion unless the solubility product is too low for this to occur (e.g. many sulphides), and in that case complexation of the metal ion by the anion of the acid, or oxidation of the anion of the salt, or both effects, will have to be brought into play. It is interesting that the dissolution of cadmium sulphide in hydrochloric acid is not simply a consequence of protonation of sulphide, but also depends on formation of chloro-complexes of the cadmium.

A few metals, owing to the amphoteric character of their oxides and hydroxides, can be dissolved in both acids and bases. In the latter case, water is the oxidizing agent.

Hydrofluoric acid holds a special position among dissolution agents. As it is a weak acid, its dissolution effect is due to the complexing properties of the fluoride ion, which are more pronounced than those of the other halides. Fluoride forms many fairly stable complexes, especially with cations of high charge density ( $Zr^{4+}$ ,  $Ti^{4+}$ ,  $Al^{3+}$ ,  $Fe^{3+}$ , etc.), the comparatively small size of the fluoride ion allowing the number of ligands to reach the maximum co-ordination number of the cation. As hydrofluoric acid reacts with silicon, it offers the great advantage of decomposing silicates and eliminating silicon from the reaction medium, by volatilization of  $H_2SiF_6$ : the drawback is that platinum or plastic vessels must be used. Hydrofluoric acid will successfully dissolve Nb, Ta or W ores that are normally resistant to attack, forming with them soluble complex fluorides or oxide-fluorides. Since under identical circumstances it forms insoluble fluorides with  $Th^{4+}$  and  $U^{4+}$ , the possibility arises of separating Nb, Ta and W from Th and U. The fluoride ion would, of course, hamper the further chemistry of a determination because of its complexing properties, but fortunately is easily eliminated by volatilization as HF on heating with sulphuric or perchloric acid; however, some elements besides silicon give volatile fluorides ( $BF_3$ ,  $GeF_4$ ,  $AsF_3$ ,  $AsF_5$ ) and may be lost in the dissolution process.

Hydrochloric acid is frequently employed for dissolving solid samples. Thus some naturally occurring substances such as the carbonates of Mg, Ca, Fe, Mn and oxides of Fe and Mn can be dissolved, but not the oxides of Al, Si, Sn, Ti. Hydrochloric acid is used mixed with boric acid to dissolve certain fluorides ( $CaF_2$ ) or mixed with oxidants ( $HNO_3$ ,  $H_2O_2$ ,  $KClO_3$ ,  $Br_2$ , etc.) to dissolve mineral sulphides.

† Strictly speaking, the proton functions as an oxidant if hydrogen is evolved in the dissolution process, and in that sense *all* acids may be regarded as 'oxidizing', but convention restricts the term to those in which the anion is the functional oxidizing agent.

Hydrobromic acid is less frequently employed but in some special cases is irreplaceable. Thus with gold, platinum and palladium in ores it forms complex bromides which are extractable into organic solvents. Likewise, used with perchloric acid it forms volatile bromides of As(V), Sb(V) and Sn(IV), which can easily be separated from the sample.

Hydriodic acid dissolves some minerals, owing to its reducing character. Thus, either alone or mixed with hypophosphorous, phosphoric or hydrochloric acid, it reduces barium sulphate to sulphide and dissolves it.

Nitric acid, alone or mixed with HCl, H<sub>2</sub>SO<sub>4</sub>, HClO<sub>4</sub> or H<sub>3</sub>PO<sub>4</sub>, dissolves certain mineral components such as sulphides, selenides, tellurides, phosphates, arsenates, tungstates, etc.

Some minerals are dissolved by use of other strong or weak acids, alone or mixed, e.g. sulphuric acid, perchloric acid, phosphoric acid and boric acid, a combination of protonation and complexation being the operative factor.

Usually, to dissolve resistant minerals, sulphuric acid is used in a mixture with other acids. Perchloric acid decomposes phosphates (monazite included), and volatilizes ruthenium and osmium tetroxides; with boric acid it decomposes fluorides; mixed with sulphuric acid it volatilizes Re<sub>2</sub>O<sub>7</sub> and separates it from molybdenite concentrates. Phosphoric acid decomposes some resistant natural oxides (U<sub>3</sub>O<sub>8</sub>, chromite, chromospinels); mixed with sulphuric and perchloric acid it dissolves iron and aluminium oxides.

Since the reactivity of mineral acids rises with temperature and pressure, wet dissolution gives better results when it is conducted in closed systems (sealed glass tubes, or autoclaves).

In the sealed-tube method, the substance and solvent are sealed in a hard-glass tube which is then placed in an open steel cylinder, or better, in a closed steel cylinder with a compensating pressure produced by placing in the steel cylinder a substance which will turn into gas on heating and give rise to approximately the same pressure as that formed by the reaction mixture inside the glass tube. Thus, temperatures as high as 300°C and pressures of 100 atm may be attained. Under these conditions of temperature and pressure and with adequate contact time (sometimes over 24 hr) the ordinary acids may dissolve the most resistant synthetic or natural substances. Thus, concentrated hydrochloric acid can dissolve natural silicates (cordierite, sillimanite, amphibole, muscovite), natural oxides (cassiterite, spinel, chromite), and oxides ignited at high temperature (Al<sub>2</sub>O<sub>3</sub>, BeO, SnO<sub>2</sub> and HfO<sub>2</sub>) which would not be dissolved in the same acid at atmospheric pressure. The possibilities of dissolution in sealed tubes are greatly increased by use of mixed solvents (non-oxidizing acids + oxidizing acids + bromine, etc.). Although sealed-tube dissolution offers many advantages, it is limited in scope because the tube is made of glass and solvents such as hydrofluoric acid or strong alkalis cannot be used; there is also the danger of contaminating the sample solution with elements from the glass tube.

Decomposition in an autoclave is more advantageous. New types of pressure

vessels with a plastic reaction vessel enclosed in a metal autoclave or bomb have been proposed, especially in silicate analysis. This new technique, still developing, did not come into wide use until the second half of the present century [186].

Even wider use of this technique has been facilitated by the development of organic polymers which can stand high temperature and pressure (Teflon, polypropylene, etc.) and has been necessitated by (a) the development and requirements of new instrumental analytical techniques (e.g. atomic-absorption spectrometry) in which high concentrations of salts in the test solution make the measurement difficult, and (b) increased demands for the determination of submicrogram amounts of elements; fusion decomposition cannot be employed because of high levels of impurities in the fusion agents, and undesirable reactions of the melt with the crucible walls.

Reaction vessels made of organic polymers offer a wider choice of solvent (including hydrofluoric acid and alkalis) which increases the number of substances that may be dissolved. However, the temperature must be kept below about 400°C and the amounts of sample and solvent small.

#### *3.1.4.2 Decomposition by Fusion*

Substances which are insoluble in water, acids or alkalis are decomposed by fusion with various fluxes. This is the most powerful decomposition procedure. The cooled melt dissolves easily in water or acids. In some instances, new solid phases may appear during the fusion, which makes it possible to separate some components in the sample during the decomposition process.

##### *Alkaline fusion*

The alkaline fluxes most frequently employed are sodium and potassium carbonate, individually or mixed. Silicate minerals are easily decomposed by this method and so are the aluminium-rich silicates as well as beryl, zircon and titanite, though with some difficulty. These last are better dissolved by fusion with hydroxides and sodium peroxide.

The decomposition with carbonates is usually done in platinum crucibles, which are now very expensive, and careful consideration has to be given to corrosion. Platinum is corroded to some extent by reaction with alkali metal oxides (resulting from thermal decomposition of the carbonates), with Fe(II) (if larger amounts of it are present in the sample) and with arsenic or phosphorus (if present in the sample).

The carbonate fusion is oxidative, especially when performed in an aerial atmosphere, but to increase the oxidative power and the ability to decompose resistant materials, nitrates, chlorates, tetraborates, hydroxides, peroxides, etc. are added to the carbonates. All these oxidative agents cause strong corrosion of platinum. Therefore, fusion with alkali metal hydroxides is best done in silver crucibles and that with peroxide in nickel or iron crucibles. However, the development of comparatively cheap zirconium and glassy carbon crucibles has led to their increasing use for fusions [189].

It should be emphasized that during fusion with carbonates, some components such as arsenic, selenium, thallium and mercury are lost by volatilization.

Alkaline fusion with carbonates may also be done with sulphur added. During the fusion polysulphides are formed, which form sulphides or thio-salts with certain elements. A subsequent simple extraction with water separates soluble from insoluble sulphides. The method is suitable for the dissolution of some minerals containing arsenic, antimony, tin, molybdenum, tungsten, vanadium, silver, germanium, etc.

#### *Acid fusion*

Potassium pyrosulphate is the most commonly used reagent. At high temperature it is dissociated into  $\text{SO}_3$  and  $\text{K}_2\text{SO}_4$ . Sulphur trioxide reacts with metal oxides to yield readily soluble sulphates (except those of Ba and Pb).

Sodium and ammonium pyrosulphate can also be used, but the former is hard to obtain and the latter is less reactive. Fusion with alkali metal pyrosulphate can be used to bring into solution iron, manganese, aluminium, titanium, zirconium, thorium, niobium and tantalum oxides as well as natural tungstates. Cassiterite ( $\text{SnO}_2$ ) decomposes only if sodium fluoride is added.

Fusion with pyrosulphate is best done in silica crucibles, though porcelain and (up to about  $600^\circ\text{C}$ ) borosilicate glass can also be used. Gold, iridium, platinum and corundum crucibles are also used but are slightly attacked.

Potassium hydrogen fluoride and more rarely ammonium or sodium fluorides effectively dissolve resistant minerals such as oxides, phosphates (monazites, xenotime), silicates, niobates, tantalates, etc.

Sodium or lithium fluoborate will easily decompose mineral oxides such as corundum, spinels, cassiterite and rutile, as well as a series of resistant silicates such as cyanite, sillimanite, andalusite, topaz, staurolite, tourmaline and zircon. Fusion with borates and boric acid is similarly effective.

After the fusion, it is usually necessary to eliminate silicon, fluorine and boron by volatilization as  $\text{SiF}_4$  and  $\text{BF}_3$  by fuming with sulphuric acid. It is noteworthy that the alkali metal tetraborates are employed in preparation of samples for examination by instrumental methods such as emission spectroscopy, X-ray fluorescence spectrometry, flame spectrometry, etc. The matrix effect is reduced in this way.

#### *Reductive fusion*

When fusion occurs in presence of a reductant, e.g. carbon, several cations may be reduced to the metal and form binary or ternary alloys. This is most favourable for metals of high density which settle at the bottom of the reaction vessel and after cooling of the melt may easily be separated from the rest by mechanical means. This kind of fusion applies mainly to separation and determination of noble metals such as gold, silver and the platinum metals. Since the amount of noble metals in ores is low, they are collected in a 'button' obtained by adding lead oxide to the fusion mixture.

### 3.1.4.3 Other Decomposition Procedures

Decomposition by fusion requires large amounts of reagents and as these are not always pure the danger exists of contaminating the sample. Further, as fusion usually requires a high temperature, unwanted reactions of the melt with the crucible walls may take place. To avoid these drawbacks the sintering method is often used, which requires a minimum amount of fusing agent but does not involve fusion, i.e. it is done at lower temperatures. Thus, the Lawrence Smith method, used for decomposition of silicates in determination of alkali metals, is based on sintering with calcium carbonate and ammonium chloride. Calcium oxide, formed during the heating, is highly reactive and gives rise to insoluble silicates, borates, phosphates and sulphates. Thermal dissociation of the ammonium chloride produces hydrogen chloride which reacts with the alkali metal ions. An advantage of the decomposition, compared with dissolution procedures, is the complete separation of magnesium, but the method is notorious for incompleteness of extraction of the alkali metals, and is now seldom used.

Other sintering agents include sodium carbonate, alone or mixed with the oxide of a bivalent metal (Ca, Mg, Zn), sodium peroxide, etc. Even the most resistant minerals, such as silicates, oxides, sulphides may be decomposed.

Pyrolysis can be used for decomposition of some substances. Thus, heating organic substances or certain ores (carbonates, sulphates), will liberate volatile components such as water, carbon dioxide, sulphur oxides, which can be trapped and determined. Some metals such as mercury, lead and tellurium are also volatilized on heating and may be trapped.

Other methods such as pyrohydrolysis and ion-exchange are used for the decomposition of some solid samples and for the separation of some components in solution, but are of more limited scope.

Organic compounds may be decomposed by combustion in an atmosphere of oxygen, under dynamic (e.g. combustion train methods) or static (e.g. Schöninger flask) conditions.

## 3.2 BLACK-BOX

A hundred centuries of the Gods are not sufficient to describe the wonders of the Himalaya (Sanskrit saying)

It is a very difficult problem for the analyst, after taking the sample, to find the best method, in terms of simplicity, speed and accuracy, for establishing the composition and nature of the material to be analysed.

At the beginning of this century, the number of analytical techniques available was very limited, and only the most important components of the sample were determined. The techniques now at the analyst's disposal have greatly increased the scope of analysis. For example, the need to determine very small amounts of components of a sample has led to a well-defined branch of analytical

chemistry, namely trace analysis. Further, until recently the major emphasis in trace analysis was on the determination of inorganic species, but it is now realized that many of the most pressing problems require competence in trace organic analysis, to protect our health and environment, and to ensure the purity and nutritional value of our food.

This task is further complicated by the fact that trace inorganic analysis is mainly concerned with elemental analysis for a finite number of elements, whereas the number of organic compounds of analytical interest is almost unlimited [190].

The diversity of the samples to be analysed, together with the multitude of analytical techniques and instruments available, poses the analytical chemist a series of problems to be solved for the desired result to be obtained. The analyst must choose the best combination of man, method and instrument for production of the desired result.

We shall try, in the following sections, to make a systematic and critical study of analytical methods. This does not mean that we shall present in detail all analytical methods extant. That is the province of treatises and handbooks. What it does mean is that we shall try to distinguish between the useful and the futile [191, 192].

The analytical methods may be divided into two groups: those for determination of composition, and those for establishment of structure or for identification.

This classification is necessary because there are many chemists (and, sad to relate, many analysts) who consider structural analysis as belonging to physical chemistry instead of analytical chemistry. It is nevertheless very clear to the unbiased that both the elemental and the structural analysis of organic and inorganic compounds belong to the same discipline, namely analytical chemistry.

The purpose of this section is to present a comparison of a limited number of methods used for compositional or structural determinations, and chosen according to their importance in analytical practice. It is intended to serve the students or specialists who wish to discuss and to analyse other analytical techniques.

To obtain the desired analytical information, expensive and sophisticated instrumentation is often needed. Not long ago, Laitinen observed [193], "Looking at the past several decades of analytical instrumentation, one gets the impression that the trend toward complexity is not a linear but an exponential function of time. It is not difficult to recall examples of compounded intricacy that seem to support the idea of the toy theory".

We must not forget a matter of particular importance for the analyst, namely that irrespective of its degree of sophistication or automation, a laboratory instrument will be used, according to the nature and complexity of the sample, in order to obtain optimal analytical information in the shortest period of time. We shall emphasize this in what follows, giving some examples.

### 3.2.1 Composition

#### 3.2.1.1 *Gravimetric and Titrimetric Analysis*

To many ‘modern’ analytical chemists it will be anathema that at the start of the ninth decade of the 20th century, in a critical study of the performance of analytical methods, gravimetric and titrimetric methods are discussed first, since they will regard these methods as obsolete. However, the goal of this book is education in analytical chemistry, and such chemists as these are greatly in need of education. For one thing, a survey has shown that the most frequently used method of analysis is titration [194]. For another, without these classical methods, our knowledge of chemical reactions and chemistry would scarcely have advanced beyond the phlogiston theory, and chemical technology would still be in its infancy.

In our opinion, these methods, which seem to the specialists old and obsolete, remain valid as control methods and for establishing the analytical standards on which practically all instrumental methods depend. Erdey remarked [195] “These modern methods, however, are without exception comparison methods, which are dependent on the use of classical analytical methods for standardization purposes”.

The gravimetric and titrimetric methods will always play an important role in the educational process and must have their place in the teaching of analytical chemistry. In any chemistry course, they provide almost the only part in which physical, inorganic and organic chemistry are brought together to show how the apparently autonomous branches of chemistry really form part of the whole, which according to tradition must necessarily be more than the sum of its parts: analysis is the only unifying branch of chemistry [196].

Anyone claiming the proud title of ‘analytical chemist’ must of necessity be fully knowledgeable in the whole range of techniques available, which includes the classical methods.

Of course, rapid and automated methods of analysis are attractive, but their novelty must not be allowed to sway judgement and obscure the fact that they are not necessarily the best for a particular purpose (or, indeed, even the fastest – some classical analyses can be completed in the time it takes for an instrument even to ‘warm up’!).

In a book which is now classical, Kolthoff and Sandell [197] remark “Anyone who has acquired sufficient skill to make an exact analysis satisfactorily can adapt himself to the performance of a less accurate one – but the reverse is not true”.

The gravimetric and titrimetric methods of analysis demand three things from the chemical analyst:

- (a) knowledge of the sample to be analysed;
- (b) knowledge of the chemical reactions involved;
- (c) knowledge of the necessary laboratory techniques.

Point (a) is valid for all analytical methods, especially for the destructive methods of analysis, involving decomposition of the sample. All three requirements are interdependent, especially when the classical methods are used.

The analyst using or developing gravimetric or titrimetric methods must know thoroughly the general theory of analysis as well as the basic principles of inorganic, organic and physical chemistry.

Precipitate formation is probably the most wide-reaching type of chemical reaction in solution. The knowledge accumulated in this field has led to a diverse series of analytical techniques such as thermogravimetry, amperometric titration, and use of ion-selective electrodes with solid membranes.

The knowledge of the chemical reactions useful in analytical chemistry and the study of their mechanisms have enlarged the limits of their application and of the sensitivity of gravimetric and titrimetric methods. In this connection it is sufficient to mention complexometry and catalytic titrations. It has been said that we already know enough chemistry to solve any analytical problem, but what we lack is the ability to see how to apply that knowledge [198]. It is the function of education to supply that ability.

Apart from their direct analytical application and utility, the classical methods also play an essential role in preparation of analytical standards. Two fundamentals of all analysis, which cannot be separated from one another, are the analytical balance and the analytical standard. It has been commented that "For some reason, standardization has come to be associated with titrimetric analysis, probably by association of ideas from the term standard solution, but it can refer not only to reagents but also to apparatus, to methods, and perhaps even to the analysts themselves" [199].

It must be emphasized that the gravimetric and titrimetric techniques have played a preponderant role in the preparation and especially the analysis of standard reference materials, i.e., alloys, metals, rocks, slags, ores, biological materials, etc. These methods are, of course, used mainly for the exact determination of the major and some of the minor constituents of the sample, the purpose for which they are best suited. Various factors such as the solubility of precipitates and the values of equilibrium constants often – but not always – make it impossible to use these methods for accurate trace analysis, unless some sort of preconcentration and separation technique is applied to a large sample (a field that is largely unexplored). For these reasons, and also because they provide a higher precision and accuracy for routine determination of major elements than any of the instrumental methods, the classical methods are still very much alive. Because of their role and value in analytical chemistry, these methods must be dealt with in lectures to students and correlated with the newest methods of analysis.

To convince the young student of the proper role of the various methods – both old and modern – that are available, it is necessary to describe to him both

the theoretical principles and the practical application of these methods. However, an excess of theory or practice should be avoided. The material taught must be 'purified', just like a precipitate, by removal of any kind of informational irrelevance ('contamination').

An example of such a 'purification' was "Quantitative Inorganic Analysis" by Belcher, Nutten and Macdonald [200]. This book dealt mainly with the theory and practice of gravimetric and titrimetric methods. It should convince any unwilling beginner or cavilling 'modernist' of the role and importance of these methods as analytical techniques.

To the older analytical chemists it is well known that certain books mark an epoch. Such books were those on qualitative and quantitative analytical chemistry by Treadwell, which taught the importance of knowledge of the chemical reactions used in analytical practice, as well as the necessary accuracy of quantitative determinations, and showed that the classical techniques represent a true art by means of which the analyst may obtain, using appropriate laboratory equipment, analytical results practically free from error. Treadwell was born in New Hampshire in 1857, completed his education in Germany, and after working under Bunsen and Victor Meyer, was made professor of analytical chemistry at Zurich, where he remained until his death in 1918. These biographical details are mentioned to show the working atmosphere and tradition in which his books were written.

We shall now present particular examples of gravimetric and titrimetric methods, some of them often neglected by teachers, with remarks on their educational features.

We will begin by reiterating that analysis is the only branch of chemistry which systematically uses the other three branches and demonstrates repeatedly their interrelationship. Several examples of this have been given elsewhere [196], and here we will mention only a few ideas that seem to us fruitful for education of students. One of the criticisms made of chemistry by students is that it needs an enormous body of facts, and that much of the theory seems disjointed in the sense that there is sometimes no apparent connection between one bit and another. It is therefore important for teachers to do all they can to show students where cross-connections can be made (and it is not necessary to be an educational psychologist to realize that the more cross-links there are, the more likely it is that the appropriate memory triggers will be activated). Flinselwood's book on physical chemistry [201] is an outstanding example of what *could* be done, and the text on inorganic chemistry by Phillips and Williams [202] is also a most useful exposition of interconnections.

Analytical chemistry also has its 'statesmen' capable of a synoptic view and with the ability to put it on paper. The names of Laitinen [203] and Ringbom [204] immediately spring to mind. Ringbom's outstanding achievement was to take the ideas underlying the effect of protonation etc. on solubility, together with the concept of apparent stability constants of complexes, and show how a

single approach – the ‘side-reaction coefficient’ method – could be used to deal with these and all other phenomena in which the conditions used may affect the result. Another unifying approach that can be taken is to buffers, indicators and titration curves for weak acids, where it is easily shown from the Henderson-Hasselbalch equation that an indicator can be regarded as a buffer of extremely small capacity, and that the same pH vs degree of neutralization plot will serve for all three systems. It is then easy to show by analogy that similar considerations apply to complexometric and redox systems, and that the titration curves have the same general shape because the underlying equations have the same form:

$$\alpha = b + c \log \frac{d}{e} \quad (3.9)$$

Entropy is a highly fruitful source of material for giving students insight into chemical systems, since it is often the decisive factor in a chemical reaction system. Ellingham diagrams, for example, can be used to explain the choice of conditions for ignition of precipitates collected on paper. DCTA complexes are generally more stable than EDTA complexes because of an entropy effect, and it is the entropy change which is responsible for formation of the EDTA complexes of aluminium, magnesium and zirconium. The effect of substitution of electron-withdrawing groups on the dissociation constant of acetic acid is also an entropy effect. Steric effects and hydrogen-bonding play a significant role in deciding the stability of many complexes, and most organic reagent systems for determination of metals can be used to illustrate the interplay of physical, inorganic and organic chemistry in the design of a successful analytical procedure.

It is well known (but frequently forgotten!) that analytical chemistry provides an unrivalled opportunity for teaching inorganic reaction chemistry, and that qualitative analysis – *if taught properly* – gives the student the opportunity to exercise his powers of observation and deduction to the full. The vitality of reaction chemistry and qualitative analysis is demonstrated by recent books on these topics [205–207]. In honesty it must be admitted, however, that if qualitative analysis is taught badly (i.e. simply as use of ‘the tables’) it can be not only uneducational but also likely to give a student a dislike for analysis, or even for chemistry. The answer is simple of course: the teaching of analysis should be done only by enthusiastic experts and not left to someone who is as uninterested in the subject as he is ignorant of it.

We will now discuss in some detail two topics that well illustrate our argument that analysis is the meeting point of the other branches of chemistry.

#### *Precipitation from homogeneous solution*

This technique is based on the slow generation of one constituent of the precipitate within the solution itself. The rate of increase of the reactant concentration

can be regulated, and therefore this technique is kinetically controlled precipitation. The precipitant is produced *in situ* homogeneously throughout the solution as the result of hydrolytic, synthetic, or redox reactions. This technique offers the advantage that the precipitates formed are less bulky and have higher purity.

It was first described over a hundred years ago by Chancel [208], who recommended sodium thiosulphate for the precipitation of aluminium as the hydroxide, though he did not present the method as precipitation in a homogeneous system, and a century elapsed before its rediscovery by Willard and its subsequent development by Gordon and his school [209]. The precipitates produced by this technique are usually denser and more easily filtered off, occlusion of impurities is reduced, and larger amounts of material can be handled with improved separation from potentially interfering ions. However, the technique can result in thin films of precipitate being formed on the beaker walls, and these can be difficult to remove, and the wary analyst will always check to ensure that this has not happened. Another pitfall for the uninformed is that a sufficient excess of parent reagent and adequate reaction time must be allowed when it is the precipitant that is produced. Even an elementary knowledge of kinetics should reveal that the smaller the concentration of reagent the longer it will take to produce a given amount of product from it. The technique also has the great disadvantage of being much slower than the traditional precipitation methods.

There are various methods for precipitation in homogeneous medium.

(i) *Increase in pH.* Most precipitates formed by use of organic reagents are in effect salts of weak acids, and hence are produced quantitatively only within a certain pH-range, the lower limit being set by the protonation constants of the ligand and the side-reactions of the cation with hydroxide ions and any other anions present, and the upper limit by the side-reactions of the cation and possible further dissociation of protons from the ligand. Hence precipitation can be made to occur by controlled increase of the pH of a homogeneous solution that is initially too acidic for precipitation to occur, usually by the hydrolysis of a suitable substance. Urea is probably the most useful substance and very often used, but hexamethylenetetramine (urotropine) is also popular.



In principle, the same technique can be used to form precipitates of hydrated oxides, but experience has shown that it is better to form a basic salt, and that often a specific anion is needed if a satisfactory precipitate is to be obtained. Thus Willard and Gordon [210] found that in the precipitation of thorium by the urea method, formate will give dense precipitates but acetate will not.

(ii) *Anion release.* This method is somewhat restricted by the lack of suitable parent compounds, e.g. esters and amides, which should preferably but not necessarily be water-soluble, and which must hydrolyse at a satisfactory rate in solution. Most interest has been shown in the precipitation of sulphides by use of thioacetamide as reagent [211]. Sulphamic acid and dimethyl sulphate are used in precipitation of barium, and dimethyl oxalate has been used for precipitation of calcium.

(iii) *Cation release.* Precipitation from homogeneous solution can be brought about by the controlled release of the cation from stable complexes in a solution containing the precipitant anion. The release may be achieved by destruction of the complexing agent (e.g. oxidation of the organic moiety of an EDTA complex, or formation of cyanhydrin from a cyanide complex), protonation of the complexing agent (provided this does not also protonate the precipitant anion!), or replacement of the cation by another cation forming a more stable complex but not reacting with the precipitant.<sup>†</sup>

(iv) *Reagent synthesis.* This is based on *in situ* synthesis of an organic complexing reagent. The best example is the reaction between biacetyl and hydroxylamine to produce dimethylglyoxime for the precipitation of nickel and palladium.

(v) *Precipitation from mixed solvents.* This method works only for organic chelates of metals, the original solution containing all the reagents and sufficient water-miscible organic solvent (more volatile than water; usually acetone), to keep the metal chelate in solution. The solution is then heated to volatilize the organic solvent preferentially and so cause precipitation.

(vi) *Valency change.* The controlled change of the oxidation state of an element has frequently been used to bring about precipitation from homogeneous solution. For example, the reduction of copper(II) to copper(I) with hydroxylammonium chloride occurs slowly in acetate media, and this has been applied to the precipitation of copper(I) thiocyanate from homogeneous solution.

Precipitation from homogeneous solution has been reviewed by Cartwright *et al.* [212], and Table 3.3 gives a survey of systems available for inorganic ions [213, 214].

### *Titrations in non-aqueous media*

Many titrations are impossible to perform in aqueous medium, because either the substance is insoluble or the equilibrium constant for the reaction is not high enough. Such titrations often become possible if a different solvent is used. Vorländer [215] was the first to use a titration in non-aqueous medium. In 1903

<sup>†</sup>Strictly speaking this will count as precipitation from homogeneous medium only if the replacement reaction is slow enough for all the replacing cation to be added before precipitation begins.

he titrated aniline with hydrochloric acid dissolved in benzene. Even today, many analytical chemists consider this method as unimportant, although its utility has been proved time and again, for the determination of compounds sparingly soluble in water or too weak for successful titration in aqueous medium. Little attention is paid to this kind of titration in most textbooks on titrimetric analysis or in practical courses for students.

Table 3.3

Precipitation from homogeneous solution [213, 214]\*

(Reprinted with permission from *Anal. Chem.*, 1966, 38, 469R and *Anal. Chem.*, 1968, 40, 608R. Copyright by the American Chemical Society.)

Element	Technique	Conditions	Separation†
Barium	Anion oxidation and cation release	$\text{Na}_2\text{SO}_3$ , $\text{H}_2\text{O}_2$ , EDTA, $\text{NH}_3\text{-NH}_4\text{OAc}$ , pH 10	Ca, Fe, Mg, Pb —Sr
Beryllium	Hydrolysis	Acetylacetone, ethylenediamine, pH 9.7, 80°C	Ca, Cu, Fe, Mg —Al
Cerium	Photochemical reduction	$\text{KIO}_4$ , mercury lamp, 0.4M $\text{H}_2\text{SO}_4$	Y, Nd
Copper	Hydrolysis	8-Acetoxyquinaldine, pH 6, Al dried, 130°C	Al
	Synthesis	Phenylhydroxylamine, $\text{NaNO}_2$ , 0.1M HCl, 5°C	Ag, Ni, Zn
Indium	Hydrolysis	8-Acetoxyquinaldine, pH 4.5, 80°C	Al, Ca, Mg, Pb —Al, Ga
Iron	Hydrolysis	<i>S</i> -2-Pyridylthiuronium bromide, citrate, $\text{NH}_4\text{SCN}$ , pH 4	Al, Ca, Th, Ti —(Co, Cr, Cu, Mn, Ni, Zn)§
Lead	Anion oxidation	Sulphamic acid, $\text{HNO}_3$	Al, Cu, Fe, Mn, Ni, Zn
Nickel	pH increase	1,2-Cyclohexanedione dioxime, acetamide, pH 1.2, 90°C	Many metals
	Enzymatic hydrolysis	Dimethylglyoxime, urea, citric acid, 0.01% urease, pH 4.4, 35°C	As, Cd, Fe, Pb —Co, Hg, Pt, Te
	Synthesis	Salicylaldehyde, $\text{NH}_2\text{OH}$ , tartrate, pH 6, 25°C	Al, Cr, Fe, Mn, Zn (-Cd)‡, Co, Cu
Palladium	Synthesis	Salicylaldehyde, $\text{NH}_2\text{OH}$ , 0.4M $\text{H}_2\text{SO}_4$	many metals —Cu

Table 3.3 (continued)

Element	Technique	Conditions	Separation†
Thorium	Photochemical reduction	$\text{NaO}_4$ , mercury lamp, 1M $\text{HClO}_4$	Fe, Ti, Zr
Titanium	Cation release	$\text{H}_2\text{O}_2$ , pH 2.5	Mn, W
	Synthesis	Phenylhydroxylamine, $\text{NaNO}_2$ , tartrate, 0.5M $\text{H}_2\text{SO}_4$ , 0–5°C	$\text{Al, PO}_4^{3-}, \text{VO}_3^-$
Uranium	Volatileization of solvent	8-Quinolinol, acetone, EDTA, pH 5.8	Mg, Pb, Th
	Synthesis	2-Naphthol, $\text{NaNO}_2$ , $\text{HOAc}$ , 5°C	Al, Ca, Ce, Mg, Pb
Zinc	Hydrolysis	8-Acetoxyquinaldine, acetone, tartrate, pH 6.5	Al —Mg
Zirconium	Synthesis	2-Naphthol, $\text{NaNO}_2$ , $\text{HOAc}$ , pH 2.3, 5°C	Al, Ca, Ce, La
	Synthesis	1-Hydroxy-2-propyl-mandelate, 5–6M HCl, 85°C	Al, Fe, Th, Ti
	Synthesis	Phenylhydroxylamine, $\text{NaNO}_2$ , NaF, EDTA, 1M $\text{H}_2\text{SO}_4$ , 5°C	$\text{Cu, PO}_4^{3-}, \text{Ti}$

\* The references to the determination can be found in the original publications [213, 214].

† A negative sign indicates interference.

‡ Interference removed by masking.

§ Interference removed by change in procedure.

The role of organic solvents in the various domains of analytical chemistry is generally well known but there are few good books dealing with this subject. A remarkable and still very useful book is that of Charlot and Trémillon [216] on the theory and application of chemical reactions in various solvents and molten salts. The application of non-aqueous media in the titrimetry of organic compounds is still expanding, as witnessed by the biennial reviews in *Analytical Chemistry* [217], its development being stimulated by the demands of the pharmaceutical and petrochemical industries.

To work in this domain it is necessary to know well the theory of chemical reactions in non-aqueous media. There are some excellent books, such as those of Gyenes [218] (which gives a masterly account of the theoretical aspects and applications) and Kreshkov [219] (which gives in a short space an interesting

introduction to this subject). For the student, however, the best account is perhaps that by Budevsky [220].

Kreshkov [221] has remarked that the development of the theory has resulted in the successful differential titration of multicomponent mixtures. This is illustrated in Fig. 3.6.

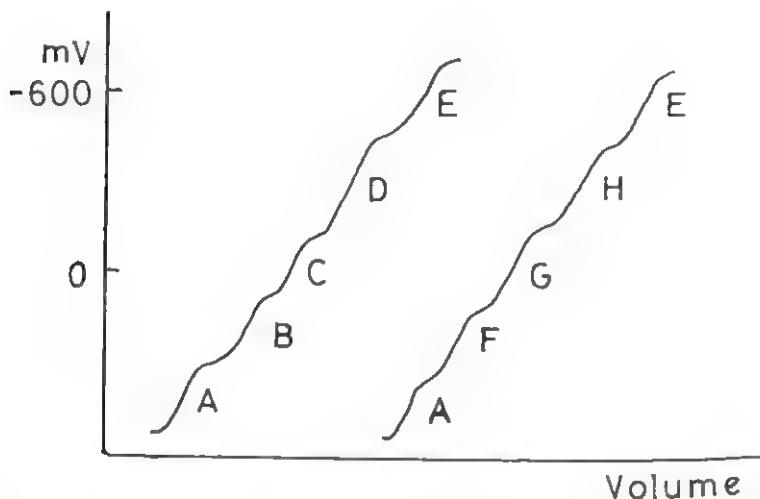


Fig. 3.6 Potentiometric titration curves of multicomponent mixtures of acids in methyl ethyl ketone medium. A -  $\text{HClO}_4$ ; B -  $\text{HCl}$ ; C -  $(\text{COOH})_2$ ; D -  $\text{HOOC.COOC}^-$ ; E - 1-naphthol; F -  $\text{HNO}_3$ ; G -  $\text{CCl}_3\text{COOH}$ ; H -  $\text{CH}_3\text{COOH}$ .

The theory today is developed to such an extent that it is possible with a reasonable degree of certainty to predict the behaviour of a substance dissolved in a given solvent, to explain theoretically the processes involved in the titration of different solutes, to choose the best solvent and titrant for a specific titration, and to make quantitative predictions, etc.

A particularly important physical quantity for choice of the solvent is the relative scale of acidity,  $E_s$ , of the solvent to be used. This is expressed as the difference (in mV) between the half-neutralization potential,  $E_{\frac{1}{2}, \text{BOH}}$ , of a strong base (e.g. tetraethylammonium hydroxide) and the half-neutralization potential,  $E_{\frac{1}{2}, \text{HAn}}$ , of a strong acid (e.g. perchloric acid):

$$E_s = E_{\frac{1}{2}, \text{HAn}} - E_{\frac{1}{2}, \text{BOH}} \quad (3.12)$$

Analytical chemists are able to judge the acid-base properties of solvents by the length and position of the relative scale of acidity (Fig. 3.7).

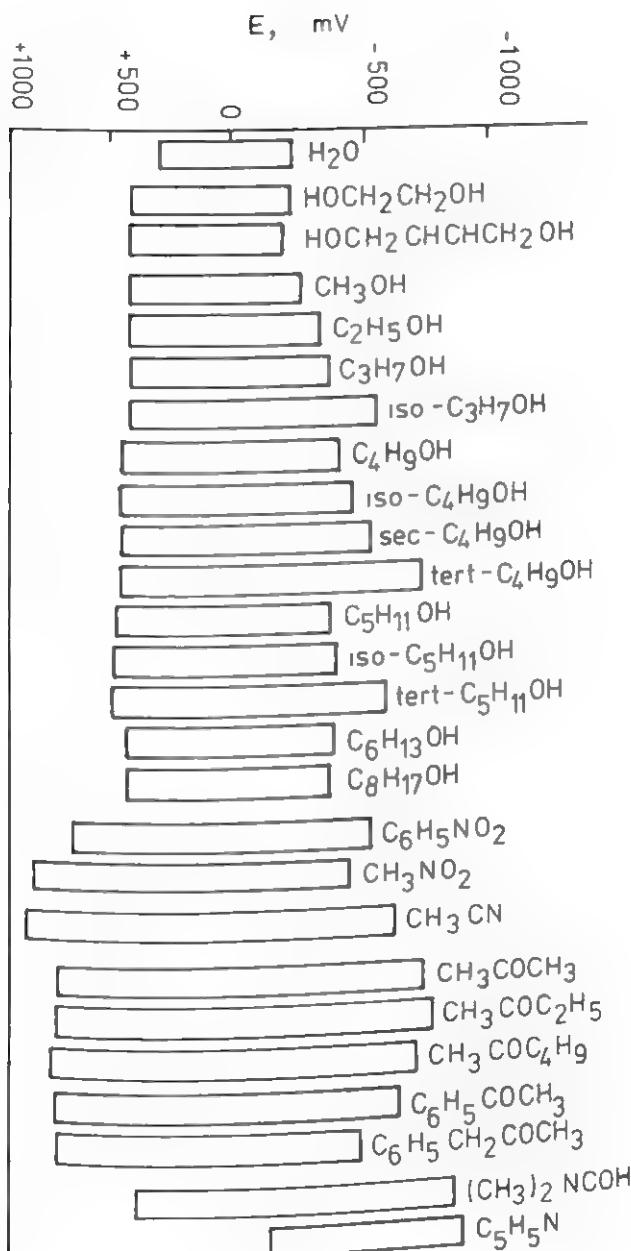


Fig. 3.7 - Relative scale of acidity of some non-aqueous solvents [221] (by permission of the copyright holders, Pergamon Press, Oxford).

They are also able to choose the best solvent or mixture of solvents to be used for titration of multicomponent mixtures of electrolytes displaying acidic or basic character (Fig. 3.8).

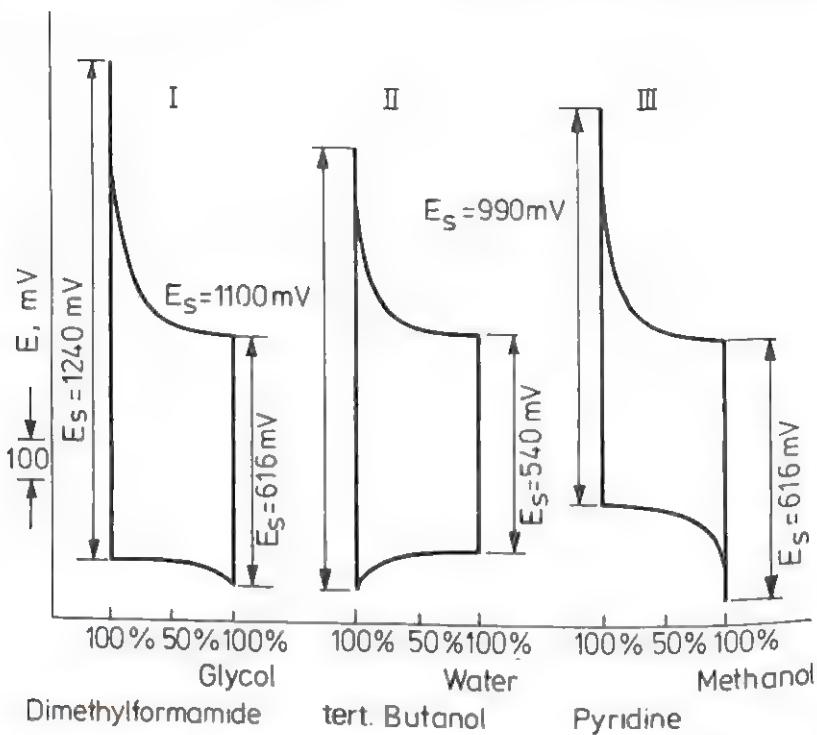


Fig. 3.8 The change of relative acidity scale of mixed solvents. I, Dimethylformamide + glycol, II, tert. butanol + water; III, pyridine + methanol [221] (by permission of the copyright holders, Pergamon Press, Oxford).

The latest development is the study of use of ion-selective electrodes to extend the scope of application of titrimetry in non-aqueous media. A recent book on applications of ion-selective membrane electrodes in organic analysis [222] includes a chapter on this topic, covering the use of glass electrodes, resin-membrane electrodes and homogeneous and heterogeneous membrane electrodes.

### 3.2.1.2 Atomic-Absorption Spectroscopy and Anodic Stripping Voltammetry

These methods are completely different in principle. They will be compared here because their performance is similar and they complement each other. Their most important feature is the particularly high sensitivity, which makes them appropriate for trace analysis.

Atomic-absorption spectroscopy and the complementary technique of flame photometry are derived in principle from the flame studies made by Kirchhoff, Bunsen and Teclu.

In an excellent book Mavrodineanu and Boiteaux [223] discuss in detail the characteristics of the flame, and the equipment and applicability in analytical practice of the flame techniques. Curiously, these authors pay little attention to the work of Teclu, whose name is now mainly associated with the widely used Teclu burner, although he published a great deal on flame and combustion processes [224].

Because flame emission spectroscopy is limited to the relatively small number of elements which can be excited at flame temperatures, this technique (in vogue in the period 1930–1950) became regarded as semi-obsolete. Efforts were made to produce higher temperatures by use of cyanogen-oxygen, hydrogen-perchloryl fluoride ( $\text{ClO}_3\text{F}$ ) or hydrogen-fluorine flames, and increase the number of elements that could be determined, but were not completely successful, owing to the technical difficulties and limited performance.

It was necessary to find similarly simple methods that would be applicable to a large number of elements.

Atomic-absorption spectrometry (AAS) was introduced as an analytical tool by Walsh [225, 226] in 1953 and by Alkemade and Milatz [227, 228] in 1955. Winefordner *et al.* [229, 230] reported the first successful analytical application of atomic-fluorescence spectrometry (AFS) with the determination of zinc, cadmium and mercury (though again the phenomenon had been known since the late 19th century). In 1959 L'vov began to publish his classic work on the application of electrothermal excitation for quantitative atomic-absorption analysis [231] (the carbon furnace method). Massmann [232] described his graphite tube system for use in both AAS and AFS, and West [233] developed the carbon-rod atomizer system.

Though many books and reviews on atomic-absorption spectroscopy have appeared, the number on anodic stripping voltammetry is very small. Among the books devoted to atomic-absorption spectroscopy, we may mention the book by Kirkbright and Sargent [234] and the monograph by Fuller [235] on electrothermal atomization. The first book on stripping voltammetry was by Brainina [236] and was followed by the excellent book on electrochemical stripping analysis by Vydra *et al.* [237]. Of these techniques, anodic stripping voltammetry (ASV) has become important because of its sensitivity and its wide applicability in trace analysis at the ng/ml level.

ASV has a lower detection limit than most other electrochemical methods of analysis, being a two-step method with a preconcentration stage. The analyte is reduced (electro-deposited, plated) onto or into the working electrode and is then oxidized (stripped, electrolysed) back into the electrolyte solution [238]. Because of the concentration step, the determinations by anodic stripping voltammetry have detection limits lower than those of flame atomic-absorption spectroscopy and comparable with those of the electrothermal atomic-absorption methods.

We shall compare the performances and deficiencies of these methods.

An interesting study of this subject has been published by Cahill and Van Loon [239].

We shall use for comparison the detection limits, the selectivity and the range of applicability in order to evaluate the analytical usefulness of these methods.

### *Detection limits*

Non-flame (electrothermal excitation) AAS has been shown experimentally to give lower detection limits than flame AAS, for most elements. Some examples are given in Table 3.4.

**Table 3.4**  
**Comparison of detection limits (ng/ml) [238]**  
 (Reprinted with permission from *Anal. Chem.*, 1974, 46, 1257A.  
 Copyright by the American Chemical Society.)

Element	ASV		AAS	
	Differential pulse	Linear scan	Flame	Nonflame
Bi	...	0.01	46.0	3.0
Cd	0.005	0.01	0.7	0.01
Cu	0.005	0.01	2.0	0.3
Ga	0.4	...	38.0	...
In	0.1	...	38.0	...
Pb	0.01	0.02	15.0	0.5
Rh	...	10.0	30.0	...
Sn	2.0(ac)	...	30.0	0.1
Tl	0.01	0.04	13.0	1.0
Zn	0.04	0.04	1.0	0.008

This table also shows that the detection limits of ASV are close to those of non-flame AAS, and that differential pulse stripping (DPASV) gives lower limits than scan stripping (LSASV). These facts are particularly important in connection with the applicability of non-flame AAS and ASV. The methods are complementary and can be used to check each other in trace analysis.

Non-flame AAS has a great advantage over ASV when the volume of sample to be analysed is very small. Although under special conditions ASV can be applied with volumes of sample as small as 100 µl, the volume of solution needed is usually 1-50 ml, similar to that for flame AAS. The volume required for electrothermal AAS is only 5-100 µl, making this technique advantageous when only a limited amount of sample is available. Against this, however, we have to set the difficulty of measuring out such small volumes with adequate

precision, and even with microprocessor-controlled dispensers, precision of sample volume becomes a limiting factor in the overall precision.

Because of the similar sensitivity of ASV and non-flame AAS, many research workers use both techniques for the same sample, in order to ensure the reliability of the analytical information. For example, blood samples have been analysed by the electrothermal method and the results compared with those obtained by anodic stripping voltammetry. As shown in Table 3.5, good agreement was obtained.

**Table 3.5**

Lead determination in capillary blood samples by non-flame AAS and anodic stripping voltammetry (ASV) [240] (by permission of the copyright holders, Elsevier Publishing Co., Amsterdam).

Sample no.	Non-flame AAS	ASV
1	49	52
2	54	54
3	61	61
4	40	41
5	41	44
6	30	26

Though in terms of detection limit there is not much difference between non-flame AAS and ASV, the latter is more advantageous in terms of multi-element analysis. ASV can be used for successive determination of some 4–6 elements in the same sample solution with no additional plating time or equipment. In applications such as this, ASV requires less time for the analysis than sequential atomic-absorption measurements. Simultaneous multielement AAS is possible but requires more complex equipment (multiple or multielement lamps, multiwavelength monochromator arrangements, etc.) [238].

Another advantage of ASV over atomic-absorption is that it can sometimes discriminate directly between various oxidation states, which is impossible by AAS unless a preliminary chemical separation is made, since as its name indicates, AAS involves neutral atoms, not ions.

A typical case is that of arsenic, for which ASV and DPASV are particularly suitable methods, and some interesting comparative work on them has been published by Forsberg *et al.* [241]. Flame atomic-absorption is relatively non-sensitive for arsenic, and the absorption line is at about 193 nm, where there is absorption of radiation by atmospheric constituents. Some procedures have also been developed which involved reducing arsenic to arsine, then determining the arsine by atomic-absorption. The arsenic may also be determined at trace levels

by neutron-activation analysis, but this requires access to a nuclear reactor and sophisticated counting equipment.

The detection limit for arsenic by both ASV and DPASV was 0.02 ng/ml. Gold was found to be superior to platinum as a working electrode material. The most satisfactory procedure for reducing arsenic(V) to arsenic(III), necessary because arsenic(V) is not electroactive, involved heating arsenic(V) with sodium sulphite in concentrated acid solution. Thus total arsenic was determined as electroactive arsenic(III) after the chemical reduction, and the arsenic(V) was found by subtracting the amount of arsenic(III) originally present (found by direct analysis of a separate sample).

### *Selectivity*

This parameter is particularly important in analysis, and must always be discussed in a comparative study of methods. If the techniques are similar in nature the comparison is easy to make, but if they are based on different principles comparison is difficult or almost impossible, because the specific conditions for each method must be taken into account. Such a difficulty occurs in the comparison we are about to make of the selectivity of AAS and ASV.

In the broadest sense, speaking about selectivity means discussing any factor that can cause interference in the determination, and the means available for preventing interference, i.e. improving the selectivity.

Pinta [242] has given an extremely wide-ranging account of the problem of interferences in atomic-absorption spectrometry. Flame and non-flame AAS have certain interferences in common, but there are some interferences that are specific for one or the other of the two techniques.

In flame AAS there are four main types of interference:

- (a) spectral, due to overlap of radiation or absorption or emission bands;
- (b) physical, due to change in the physical properties of the analyte solutions causing variation in the amount of solution reaching the flame in a given time; these interferences are not specific;
- (c) chemical, due to chemical reactions in the flame; these are specific;
- (d) physico-chemical, such as ionization; they depend on the chemical composition of the sample to be analysed.

Because of the narrowness of the resonance lines, spectral overlap of atomic lines is very rare, only about six cases being known, and it is usually possible to find a second resonance line suitable for the analysis, though the sensitivity may then be poorer. However, interference may be caused by molecular absorption bands of other species in the flame (which will manifest itself as an additional absorption signal) and by resonance fluorescence of the analyte (i.e. absorption and re-emission of the incident resonance radiation, resulting in a lower signal). Any emission from thermally excited analyte atoms in the flame can be dealt with by using modulated incident radiation and a detector tuned to the same frequency, which will eliminate the 'direct current' emission signal, and leave the

'alternating current' absorption signal for detection, but the molecular absorption and the fluorescence interferences cannot be dealt with in this way.

If particularly concentrated sample solutions are sprayed into the flame, two other spectral effects can arise. One is scatter of the incident radiation by the clotlets formed in the flame by evaporation of the solvent and incomplete volatilization of the solid left. This can be dealt with by use of a background correction made by measuring the 'absorption' (i.e. the scatter) at wavelengths close to the absorption line but not overlapping it. The other effect is more subtle, and is the pressure broadening or collisional damping; as a result of the polarization occurring during the collision of the analyte atom with another atom in the flame, the broadening is asymmetric, the line profile being shifted towards the long-wavelength side, resulting in lower absorption at the line centre.

In AAS (and also in AFS) the term physical interference is usually employed to denote any influence of other materials present in the sample solution besides the analyte element, on one or more of the physical processes involved during the nebulization and atomization, and dependent on one of the physical properties of the sample solution. The principal interferences result from the effect of solution viscosity on sample aspiration, and the effect of the surface tension, vapour pressure and temperature of the sample solution on the nebulization process and solvent evaporation.

The most important interferences in flame atomic-absorption spectroscopy are chemical. They may be classified into atomic interactions (in the vapour phase), and molecular interactions. The molecular interactions are practically all chemical reactions.

There are a large number of chemical interferences, the common feature being that the interfering materials affect the efficiency or extent of atom production from the analyte. The most interesting are the effects of different anions such as borates, silicates, phosphates, etc. For example, phosphate influences the determination of magnesium and the alkaline-earth metals by formation of thermally stable compounds which are resistant to atomization in the flame. Such interferences are generally overcome by the addition of excess of chemicals which release the analyte by forming a still more refractory compound with the anion, or in some cases by use of flames that are much hotter or are strongly reducing. Sometimes such interferences may be eliminated by addition of sufficient excess of the interferent to all samples and standards, thereby 'swamping' the effect of the interferent present in the sample, but there will be a loss of sensitivity.

The physico-chemical interference caused by ionization arises from the decrease in the ground-state atomic population if part of it is ionized. The problem can be dealt with by addition of a large excess of a salt of a more easily ionized metal (provided the metal does not cause other interference).

In the case of non-flame (electrothermal atomization) AAS, the types of interference are divided into physical and chemical

The physical interferences have the following sources.

(a) Sample introduction. Variation in the sample size or position can give rise to a variation in the signal response. These signal variations can be reduced by use of integration instead of peak-height measurement.

(b) Background signals. Large concentrations of matrix material vaporized during the atomization stage can cause scattering of the incident light beam. Molecular species vaporized during the atomization stage can cause molecular absorption by their broad band and line spectra. All three effects give rise to spurious analytical signals which can be dealt with in many cases by the use of background-correction techniques, but the precision will be poorer.

(c) Memory effects. Incomplete atomization of an element can cause enhancement in subsequent analytical determinations; if the element is allowed to accumulate on the atomizer unit the errors become progressively greater. This occurs especially in the determination of the elements which form refractory oxides (V, Mo, W, Zr, etc.). This effect may be eliminated to a large extent by using higher atomization temperatures or a clean-up heating of the graphite atomizer.

(d) Ionization effects.

Chemical interferences are also due to several factors.

(a) Pyrolysis losses. Losses of the analyte can occur during the pyrolysis stage if the element concerned is present in volatile form or can be converted into volatile form by the sample matrix.

(b) Anion/cation interferences. These interferences can often be minimized by close matching of standards to samples or by solvent extraction procedures.

(c) Condensation. This type of interference is particularly prevalent with the filament type of atomizer. The effect can be minimized by using the hydrogen-diffusion flame.

(d) Carbide formation. To minimize this effect it is essential to maintain the atomizer in a reproducible condition, e.g. by the use of pyrolytic coating, or to use a metallic atomizer.

(e) Nitride formation. This effect arises when nitrogen is used as the inert shield gas, but is usually negligible.

We have dwelt at length on the problem of interferences in AAS in order to demonstrate that even in the case of this technique (which was originally thought to be free from interference) the nature of the sample to be analysed may be of paramount importance and must be known by the analyst.

Anodic stripping voltammetry is also subject to a series of interferences.

(a) Overlapping stripping peaks. Use of a different electrode material or a different supporting electrolyte often eliminates this problem.

(b) Intermetallic compound formation. If mercury is the working electrode, this kind of problem is generally less severe when the concentrations of the metals dissolved in it are low.

(c) Electrode surface films. ASV peak sizes are very dependent on the

nature of the electrode surface. It is probable that this kind of effect is the reason for some non-reproducible results.

The selectivity can be improved by electrochemical means, such as increasing the selectivity of the pre-electrolysis step (e.g. by using a potentiostat when determining a metal in the presence of a more electronegative one), or choosing a more selective monitoring method for the stripping process (e.g. by using a.c. instead of d.c. voltammetry, or a galvanostatic method, or changing the electrode material).

Complexing agents provide many ways of improving the selectivity of the stripping step. Although there is a considerable literature on this in the case of mercury electrodes, fewer data are available on the effect of complexing agents on the electrode reactions of metals at solid electrodes.

### *Analytical applications*

From the point of view of analytical application, there is one factor which, in our opinion, has resulted in ASV being less commonly used in laboratory practice than non-flame AAS is, and that is that non-flame AAS is regarded as easier to use for large numbers of samples, but this is simply due to the automation of non-flame AAS being more advanced than that of ASV.

If only the sensitivity and selectivity are taken into account, both techniques are very similar in performance, the only difference being that AAS is applicable to a larger number of elements than is ASV.

The analytical applications of AAS are extremely numerous. It is not the purpose of this section to examine them in detail. We shall mention only the major applications of electrothermal atomization AAS. These are mainly in the fields of environmental and clinical analysis. Thus AAS is widely used in chemical and biochemical analysis for the major essential elements such as sodium, potassium, calcium and magnesium, the minor essential elements such as copper, zinc, iron, chromium, molybdenum, selenium and manganese, and the toxic elements such as lead, cadmium, mercury, thallium and beryllium.

Other important applications are to the analysis of foods and beverages, metals and alloys, petroleum and petroleum products, siliceous materials, soils, plants and fertilizers, waters and effluents. A short review has been published by Pye-Unicam [243].

ASV is also used extensively for trace analysis. Some examples are given in Table 3.6.

Coleman [244] makes the interesting observation that "A variety of techniques of adequate sensitivity for the trace analysis of bulk samples are available, and it is important to relate the analytical problem to the overall requirement so that a rational and economical choice can be made". For this reason it is necessary to discuss critically the various methods of analysis. We shall illustrate this with Table 3.7, where the analytical methods for pollutants are compared.

Table 3.6  
Summary of selected ASV applications [238].

(Reprinted with permission from *Anal. Chem.*, 1974, 46, 1257A. Copyright by the American Chemical Society.)

Element determined	Sample type(s)	Type of working electrode used*	Comments
Ag	Natural water	WIG	Linear scan stripping (LSS)
Au	Rain and snow	WIG & PG	Two types of graphite electrodes compared
	Drugs and serum	CP	Rotating ring disk electrode used to improve reproducibility
Hg	Natural water	WIG	
Sn	Geological materials	HMDE	Both linear scan and a.c. stripping techniques used
Zn, Cd, Pb	Sea-water	HMDF	Stripping carried out with matched Hg drops, only one of which had been used for deposition, to cancel background by difference measurement techniques
Zn, Cd, Pb, Cu	Atmospheric particulates	HMDE	LSS
	Natural water	HMDE	LSS
Pb	Estuarine waters	HMDE	a.c. stripping
	Blood	HMDE	Small samples required
	Atmospheric particulates	HMDE	LSS
Zn, Cd, Pb, Cu	Atmospheric particulates	MTFE	LSS
Zn, Cd, Pb, Cu	Natural water	MTF-L	Lability of metal complexes in water estimated
Pb	Blood	MTFI	Large electrode areas and long deposition times used to analyse trace levels in acid digests
Pb, Cu, Cd	Natural water	MTI-I	Labile and acid exchangeable metal ion concentrations determined
Cu	Secondary sewage effluents	MTFI	Sephadex used to separate molecular-weight fractions and establish that Cu occurs in two distinct fractions
Pb, Cd, Cu	Natural water and reagents	MTI-GH	Wax impregnation of electrode not required
Rh			
Pb, Cd	Natural water, blood, urine	MTI-GC MTF-GC	10 <sup>-7</sup> M Rh determined Small blood and urine samples analysed by differential pulse techniques without prior acid digestion
Pb, Cd, Zn, Tl	Natural water, blood and biological tissue	MTI-GC	Gallium added to eliminate formation of interfering Cu-Zn intermetallic

\* WIG = wax impregnated graphite; PG = pyrolytic graphite, CP = carbon paste; HMDF = hanging mercury drop electrodes; MTI-I = mercury thin-film electrodes; MTF-GC = mercury thin film on glassy carbon.

Table 3.7

Comparison of analytical methods for pollutants [244]  
 (Reprinted with permission from *Anal. Chem.*, 1974, **46**, 989A.  
 Copyright by the American Chemical Society.)

Technique	Advantages	Limitations
Microscopy	Excellent for particulate matter Identification of compound and crystalline form possible Very sensitive Rapid	Not suitable for pollutants in solution Not readily quantified Requires specialized skills and training
Atomic absorption and fluorescence	Applicable to more than 60 elements Simple spectra and instrumentation Sensitive	Simultaneous multi-element analysis difficult
Atomic emission	Rapid Multielement analysis feasible Sensitive Rapid	Flame sources have significant matrix effects
Mass spectrometry	Plasma source eliminates most chemical interferences Multielement technique Excellent sensitivity	Specialized sample preparation techniques for spark source
Neutron activation analysis	Plasma source promises rapid analysis Freedom from contamination Excellent sensitivity for some elements Applicable to wide variety of matrices	Plasma source still in development phase Limited availability for routine analysis Total time for multi-element analysis may be long
X-Ray fluorescence	Direct examination often feasible May be nondestructive	Limited sensitivity
Anodic stripping voltammetry	Multielement technique Rapid Simple technique and equipment Excellent sensitivity for some elements	Particle size effects must be carefully controlled Not suitable for wide range of elements

This table shows the advantages and limitations of many analytical methods. It can be seen that atomic-absorption and fluorescence spectroscopy as well as anodic stripping voltammetry play an important role in the analysis of inorganic pollutants.

We conclude this section by mentioning more complex techniques such as combined electro-deposition and atomic-absorption spectroscopy.

Electrochemical preconcentration techniques can be used in atomic-absorption analysis for trace metals, to eliminate interferences from high concentrations of salts, which would otherwise give rise to non-specific absorption (see p. 121).

Applications of this approach have been reported for a variety of metals [245]. In one version of the technique [246] the metal in question is deposited electrolytically on a thin metal wire and is then atomized by electrical heating of the wire. In another approach, the metals are preconcentrated on a graphite rod, which is dried and ground, and a portion of the graphite powder is finally heated in a graphite furnace [247].

These techniques utilize electrothermal atomization of the metals, after the electrochemical preconcentration step, but a flame method could equally well be used. Lund *et al.* [248] described the flame atomization of metals after electrochemical preconcentration on a platinum spiral. Table 3.8 shows that good detection limits are obtained for a series of elements added as spikes to sea-water samples, and compares them with those obtained for the Delves cup technique by Kerber and Fernandez [249].

This combined electrochemical/AAS technique is especially useful for samples having a high matrix salt concentration, such as sea-water, urine and

**Table 3.8**

Detection limits (in  $\mu\text{g/l}$ ) of the ASV technique with a 2-min electrolysis, and of the Delves cup technique [248] (by permission of the copyright holders, Elsevier Publishing Co., Amsterdam).

Element	Wavelength (nm)	ASV technique	Delves cup
Ag	328.1	1	1
Bi	223.1	150	20
Cd	228.8	0.1	0.05
Hg	253.7	100	100
Pb	283.3	5	1
Se	196.0	5	1000
Te	214.3	50	300
Tl	276.8	1	10
Zn	213.9	0.1	0.05

biological fluids, as well as inorganic materials which have been decomposed by treatment with acids or by fusion. The method is limited to the more volatile elements, but it can be seen from Table 3.8 that these include many of the toxic metals which are of particular concern in the present day discussion of environmental pollution.

### 3.2.1.3 X-Ray Fluorescence and Microprobes

These techniques provide non-destructive methods of analysis, which have the advantages over destructive methods that the analytical information obtained from the sample is 'permanent', in the sense that the analysis can be repeated on the same sample, since none is consumed, and that the sample is not contaminated by impurities in reagents (since none are used).

The discovery of X-rays by Rontgen (1895) was one of the crucial discoveries at the turn of the century, and within two decades the fundamentals of qualitative and quantitative X-ray analysis had been established by Moseley [250, 251] (1913–1914). The first commercial equipment for X-ray spectrometry appeared in 1948 [252], and rapid development followed. Castaing and Guinier (1949) built the first electron-probe X-ray primary-emission spectrometer.

The introduction of the electron probe initiated the non-destructive study of surfaces, which has developed extremely rapidly in the last three decades, because expanding industrial technology has required complete knowledge of the surfaces of the new materials being used.

Development of these powerful techniques was further stimulated by the move to thin-film technology in the semiconductor industry and by the growing technological importance of such phenomena as corrosion and catalysis. In all these areas the composition and properties of surfaces determine many of the properties of materials.

Photons, electrons, atoms, molecules and ions are all used as sample probes in the instrumentation for surface analysis. The techniques are usually denoted by acronyms, and we have Auger Electron Spectroscopy (AES), Low Energy Electron Diffraction (LEED), X-Ray Photoemission Spectroscopy (XPS), Ultra-violet Photoemission Spectroscopy (UPS), Energy Loss Spectroscopy (ELS), Field Emission Spectroscopy (FES), Appearance Potential Spectroscopy (APS), Ion Neutralization Spectroscopy (INS), Ion Scattering (IS), and Secondary Ion Mass Spectroscopy (SIMS).

At the 27th Pittsburgh Conference on Analytical Chemistry and Applied Spectroscopy (Cleveland, 1976), Rosasco *et al.* presented a preliminary report on the Raman microprobe as a new analytical tool [253]. A research group at Heidelberg have recently introduced a new technique with promising potential applications, the proton microprobe [254].

We may now ask how far the sophistication of laboratory equipment will be continued, as a consequence of the development of new analytical techniques. As teachers and research workers we must know the new techniques in the field

of analytical chemistry and select from them in order to give to the student the essence of the present 'ocean' of information. We agree with Laitinen's opinion on the proton microprobe: "In summary, the proton microprobe serves as an excellent example of a new approach which offers advantages for specific applications at the expense of disadvantages that need to be considered by the analytical chemist in deciding whether it should be added to the existing capability of analytical facility" [255].

Before making a comparison between X-ray fluorescence and microprobes, we wish to recommend to those seeking acquaintance with this fascinating domain, the excellent book by Bertin [256], which in our opinion is an essential reference book in this important field of non-destructive analysis.

It is not our purpose to advertise particular books, but our duty as teachers is to show students what and how to read, so here we pass on to teachers and beginners alike, information about books and articles we have found especially helpful. As we have emphasized, the teacher must filter the informational material, using it to induce in the student, especially the future research student, the spark of curiosity and interest in a particular field of science. Bertin's book, in our opinion, does just that.

X-Ray fluorescence (XRF) is the characteristic secondary X-radiation produced after inner-shell electrons have been removed by primary X-ray excitation [257].

Electron-probe microanalysis (EPMA), or electron microprobe analysis, is a qualitative and quantitative method based on measurement of the wavelengths and intensities of the characteristic X-ray spectra of chemical elements, excited by an electron beam about  $1 \mu\text{m}$  in diameter.

It is very difficult and almost impossible to discuss the sensitivity of all the different non-destructive methods of analysis, or even of the large variety of physical methods of surface analysis, since for a given technique it can vary from element to element or for the same element in different matrices.

Table 3.9 gives a series of sensitivities in terms of minimum detectable mass under the most favourable conditions.

From this table, the sensitivity of XRF, although in general not as good as that of optical emission spectrography, is seen to be still very high. Quite recently, however, Knoth and Schwenke [258] described an X-ray fluorescence spectrometer with totally reflecting sample support, which could provide trace analysis at the ng/g level. For a given analysis, instrument components, accessories, and conditions may be chosen to give optimal sensitivity. With a given X-ray tube target, crystal, collimator system, and detector, sensitivity for a pure analyte is a relatively simple function of atomic number. Elements having about the same atomic number are likely to have about the same sensitivity in a given system. No such simplicity exists in optical emission spectrography however, and things are even more complicated if we examine the sensitivity of the methods for surface analysis.

Table 3.9

Ultimate sensitivities of microanalytical methods for the most sensitive elements under the most favourable conditions [256] (by permission of the copyright holders, Plenum Press, New York).

Method	Minimum detectable amount, g
Microchemistry	$10^{-9}$
Polarography (voltammetry)	$10^{-9}$
X-Ray fluorescence spectrometry (XRFS)	$10^{-9}$
Optical absorption spectrometry	$10^{-10}$
Optical emission spectrography	$10^{-10}$
Auger-electron spectrometry (AES)	$10^{-11}$
Flame (atomic) absorption spectrometry (AA)	$10^{-11}$
Ion-scattering spectrometry (ISS)	$10^{-11}$
Flame emission spectrometry	$10^{-12}$
Ion-induced X-ray spectrometry	$10^{-12}$
Mass spectrometry (MS)	$10^{-13}$
Neutron-activation analysis (NA)	$10^{-13}$
Optical fluorescence microscopy	$10^{-14}$
Electron-probe microanalysis (EPMA)	$10^{-15}$
Radioactive tracer analysis	$10^{-18}$
Secondary-ion mass spectrometry (SIMS)	$10^{-18}$

The first question generally asked of a surface analysis technique is whether it can detect a certain element of interest at a particular concentration in the presence of specified matrix elements. Several aspects of elemental analysis arise in this question [259].

(a) Coverage. What elements in the periodic table can each technique detect, on the basis of the fundamental principles involved?

(b) Specificity. How well do the fundamental processes and instrumentation employed permit the detection of one element in the presence of another? In other words, is there any spectral interference?

(c) Variations in sensitivity. Are the excitation and detection of the analytical signal uniform from element to element? Changes in sensitivity from element to element complicate quantitative analysis and can make it difficult or impossible if they are not predictable or they vary with the matrix, excitation conditions, etc.

(d) Detection limits. What is the minimum concentration that can be detected in the absence of spectral interference? Elemental detection limits can be altered by variations in sensitivity and by specific spectral interference.

Table 3.10 surveys these four aspects for five techniques used for surface and thin-film compositional analysis, and some interesting conclusions may be drawn from it.

**Table 3.10**  
Elemental sensitivity [259]

(Reprinted with permission from *Anal. Chem.*, 1975, 47, 818A. Copyright by the American Chemical Society.)

Technique	Coverage	Specificity	Sensitivity variation	Detection limits (atomic fraction)
Auger electron spectrometry (AES)	Li-U	Good	Less than a factor of 10	$10^{-3}$
MeV ion back-scattering spectrometry (BS)	Li-U ( $\omega/2$ -MeV ${}^4\text{He}^+$ )	Low Z - good High Z - poor	Sensitivity increases with $Z - \text{Bi}/\text{O} \approx 100$	$10^{-1}-10^{-4}$
Electron spectroscopy for chemical analysis (ESCA)	Li-U	Good	Less than a factor of 10	$10^{-1}-10^{-3}$
Ion scattering spectrometry (ISS)	Li-U	Small $\frac{M}{m}$ - good Large $\frac{M}{m}$ - poor	Sensitivity increases with $Z - \text{Bi}/\text{O} \approx 5$	$\sim 10^{-2}$
Secondary ion mass spectrometry (SIMS)	H-U	Good (also provides isotopic detection)	Depends on ionization efficiency $10^4-10^5$	$10^{-4}-10^{-5}$

All the techniques are suitable for elements 3-92, but SIMS can also be used for hydrogen. AES and ESCA are not highly subject to spectral interference. SIMS gives excellent elemental specificity and isotopic resolution, but as with any technique, the lower the detection limits required, the greater the problem of spectral interference.

All these considerations regarding the sensitivity of XRF techniques or of the methods of surface analysis, show that a series of techniques with even higher sensitivity and specificity than X-ray spectrochemical analysis has been developed.

It should be mentioned, however, that on account of the cost of the equipment and the relative popularity of the techniques among chemists, more XRF equipment is sold than electron-probe analysers or other sophisticated apparatus for surface analysis. Even when fully automated (as in the Phillips PW-1270 simultaneous automatic spectrometer), XRF equipment is simpler than electron-probe microanalysers.

Because of the small target-area of the electron beam, problems of microhomogeneity and microtopography are severe. For X-ray fluorescence

spectrometry, polishing with 30-100  $\mu\text{m}$  grade abrasive is usually satisfactory whereas for electron-probe microanalysis, a 0.25  $\mu\text{m}$  grade abrasive or finer may be required, and there is little value in even semiquantitative comparison of intensities from specimens having substantially different degrees of polish. Also, the background is higher and much more difficult to measure accurately in electron-probe microanalysis.

Chemical effects on wavelength of maximum emission are the exception in X-ray fluorescence spectrometry but the rule in electron-probe microanalysis when the chemical state of the analyte varies among the specimens or when pure analyte is used to set the peak wavelength on the spectrometer and the specimens are compounds.

Suitable standards are much more difficult to obtain for electron-probe microanalysis because microhomogeneity is required and the standards and samples must have the same microtopography.

A limiting factor in the use of non-destructive techniques of surface analysis is the equipment itself. All the surface and thin-film analysis techniques require a high or ultrahigh vacuum and an ion source, but each makes different demands on these two components, depending on the process involved and the sample under analysis [260].

To show the performance and use of surface analysers, we shall discuss the characteristics of some of the techniques, namely: Auger electron spectrometry, Raman microprobe, alpha-induced X-ray emission, synchrotron radiation and proton microprobe.

We consider that discussion of these techniques will show convincingly that surface analysis is now of particular importance from the scientific and practical points of view.

#### *Auger-electron spectrometry (AES)*

The radiationless reorganization of atomic electronic shells was first experimentally established by Auger in 1923 [261]. The development of AES as a powerful tool for the analysis of surfaces began with the work of Weber and Peria [262] and Harris [267].

The energy and intensity of the Auger electrons can be used for qualitative and quantitative analysis of the outer atomic layers of the sample. The energy of the Auger electrons permits qualitative and quantitative analysis of the volume of the material bounded by the cross-sectional area of the primary electron-beam (diameter 5-500  $\mu\text{m}$ ) and the Auger-electron escape depth (3-20 Å). If Auger-electron spectrometry is combined with ion-beam sputtering, depth profiling analysis may be performed. The lateral resolution is determined by the diameter of the electron-beam. Scanning techniques make it possible to produce a two-dimensional map or image of the surface distribution of a chosen element. The method can be used in conjunction with 'physical' imaging by scanning electron microscopy. Recently, it has been suggested that there is considerable analytical potential for AES in the gas-phase [264].

An electron-beam of 3–10 keV in energy at a current of  $50\mu\text{A}$  is employed for producing Auger electrons from the sample surface to be characterized. The detection limits attainable by AES are related to the integration time and the excitation electron current; thus, the reduction in beam current which accompanies decrease in probe diameter will result in poorer detection limits, and increased analytical time will be needed to offset this. Because of the ultrahigh vacuum used, to obtain reasonable turn-round times a multisample carrousel or a vacuum-lock arrangement must be available.

The cylindrical mirror analyser is the most commonly used dispersing element in AES, with an electron multiplier for electron detection. Pulse counting techniques (with no spectrometer voltage modulation) have been used for detecting the low Auger intensities produced by low-intensity excitation beams.

A multiplexer or computerized data system for recording the intensities of several peaks as a function of time is essential if the instrument is to be used extensively for depth profiling. Auger microanalysis and imaging require a primary electron-beam raster and oscilloscopes for recording the read-out.

The applications of AES are now numerous, especially in surface chemistry by means of the Auger chemical shift, the adsorption and reactions of gases on a clean metal surface being the main field of research. Experiments have not been confined to the metal–oxygen system, the surface interactions of other gases having been investigated, notably CO. For example Barrie and Brundle [265] compared ESCA and Auger spectrometry for examining CO absorbed on polycrystalline molybdenum.

AES is also used for study of heterogeneous catalysis, especially correlation of the surface elemental composition of a catalyst (obtained by AES) with its performance in chemical processes.

AES is used routinely to detect surface impurities before and after cleaning. The most important industrial application of AES is in the analysis of species segregated on a surface or at the grain boundaries of metals.

The continuous removal of surface material by inert-gas ion-bombardment (ion-milling) with simultaneous AES monitoring of element concentrations on the ‘fresh’ surface is used to obtain a composition profile perpendicular to the solid–vacuum interface. This technique of depth-concentration profiling has been applied in several fields, notably to steels, alloys and electrical devices.

Surface composition has an important influence on the nature of electro-deposited material. AES has also been used in this area. Several semiconducting materials have been examined by AES for surface contamination.

In 1970 MacDonald and Waldrop [266, 267] demonstrated that a scanning electron microscope (SEM) could be interfaced with an Auger spectrometer. Elements in a particular area of a specimen were detected in point-by-point fashion by high spatial-resolution AES and presented as an Auger-electron image, which could then be compared with a conventional micrograph. AES-SEM instrumentation is used in metallurgy, study of semiconductors, forensic science and other areas.

Some advantages and disadvantages of the Auger-SEM combination are given in Table 3.11.

Table 3.11

Aspects of AES-SEM [268] (by permission of the copyright holders, Maclean-Hunter Ltd., Toronto).

Advantages	Disadvantages
High depth-resolution ( $5\text{-}10 \text{ \AA}$ )	Spatial resolution $2 \mu\text{m}$ (?)*
Low detection-limit (10–800 ppm)	High vacuum required
Non-destructive (?)*	Semi-quantitative
Detects elements with $Z \geq 3$	Surface-condition dependent
Depth-profiling can be used	Difficult to interface AES with SEM
	Slow data acquisition
	Complex instrumentation

\* Queries added from Thompson [269].

Applications of Auger electron spectrometry have been reviewed by Thomson [269]. Table 3.12 gives a comparison of the advantages and disadvantages of AES and other techniques of surface analysis.

Table 3.12

Summary of relative advantages and disadvantages of five common surface analytical techniques [259]. (Reprinted with permission from *Anal. Chem.*, 1975, 47, 818A. Copyright by the American Chemical Society.)

	Advantages	Disadvantages
AES	Sensitivity to low $Z$ Minimal matrix effects Microanalysis	Difficult to quantitate 0.1% detection limits
BS	Good all-around technique Fast Quantitative in concentration and depth	Low sensitivity, especially for low $Z$ Poor lateral resolution 0.1% detection limits
ESCA	Chemical information	Poor lateral resolution Slow profiling
ISS	Outer monolayer analysis	Low sensitivity Poor lateral resolution Slow profiling
SIMS	ppm detection limits for many elements Isotopic resolution Fast Microanalysis	Quantitation and matrix effects

### Raman microprobe

The Raman spectrum of a microscopic sample can be used to ascertain the chemical species present in inorganic and organic materials. In addition, the type of site (local or molecular environment), structural co-ordination, or phase (crystalline or glassy) in which the species is present can often be inferred. The Raman spectrum of a microparticle can be observed because to a first approximation the power of the Raman-scattered light is proportional to the total power incident on the sample, and a laser source should generate sufficient power in the Raman-scattered light to make it possible to measure the spectrum from a micrometre-size particle (laser sources can be focused so that the total power is contained in a diffraction-limited spot of the order of  $1\text{ }\mu\text{m}$  in diameter).

It is very important to optimize the optical system of the microprobe so that collection of the light scattered by the particle is maximized and collection of any radiation emitted from the substrate is minimized. To extend measurement times and obtain analytically useful data, the particle, the focused excitation beam and the collection optics must be kept very precisely aligned.

Figure 3.9 gives a schematic diagram of a Raman microprobe spectrometer.

In the microprobe, the scattered light is collected by an ellipsoidal mirror in a  $180^\circ$  back-scattering geometry and then passed into a double monochromator equipped with concave holographic gratings. The sample particles, supported by a substrate, are positioned in the laser beam on a stage driven by remote control.

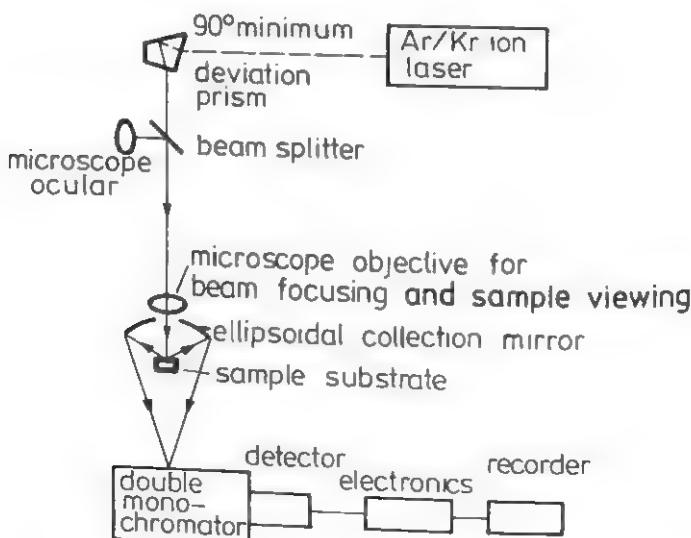


Fig. 3.9 Schematic diagram of Raman microprobe spectrometer [270]. (Reprinted with permission from *Anal. Chem.*, 1978, **50**, 892. Copyright by the American Chemical Society.)

The signal obtained from the scattered light can then be maximized by minor adjustment of the position of the particle and the excitation beam. Spectra are recorded by scanning with the monochromator and plotting on a strip-chart an analogue signal proportional to the number of photons counted in a selected measurement time at each spectral interval. Recently developments include complete computer control of positioning of the sample substrate and optimization of the alignment and measurement parameters. Various substrates have been used for fixing the particles. High-purity sapphire ( $\alpha\text{-Al}_2\text{O}_3$ ) and lithium fluoride appear to be especially good. Before sample deposition the substrate surface can be coated to form a finer grid or to change the physical or chemical behaviour of the surface.

The Raman microprobe is a valuable complement to other microprobe techniques, although there is the question of its suitability for analysis of samples previously prepared for other microprobe methods (e.g. electron-probe or ion-probe). On the other hand, because the technique is non-destructive, samples can be subsequently measured with other probes.

An interesting application of the Raman microprobe is the study of environmental airborne particulates and characterization of the secondary particulates in the size range below  $2\text{ }\mu\text{m}$ . Another important use is for characterization of species absorbed in the surface of microparticulates. The ability to detect spectral features associated with a contaminant on a single particle is a very distinct advantage of this new microprobe technique.

The Raman microprobe is extremely useful for characterizing organic particles with sizes below  $10\text{ }\mu\text{m}$ . Micro Raman spectra have been obtained from polymers, salts of organic acids and biologically significant compounds such as urea and cholesterol.

However, there are some unresolved fundamental questions about scattering from microparticulates, especially the effect of particle size or sample heating on the ultimate limits of detection. There are also questions about the relative sensitivity of this probe for surface-adsorbed species, and the quantitative capabilities of the technique.

#### *X-Ray emission induced by $\alpha$ -particles*

The recent development of a totally new  $\alpha$ -particle induced X-ray emission technique called Alpha-X (a trademark of the Kevex Corp.) has provided a non-destructive, quantitative tool in a compact unit suitable for attachment to existing surface and thin-film analysis systems or to any ultrahigh vacuum system.

The Alpha-X technique consists of detection and analysis of the X-rays from a specimen irradiated with  $\sim 5\text{-MeV}$  alpha-particles from a radioactive source.

The subsequent simultaneous, multielement X-ray energy-dispersive spectrometry for elements with atomic number  $\geqslant 6$  is best accomplished by using a high-resolution lithium-drifted silicon Si(Li) detector in the windowless mode (i.e. no barrier between the specimen and the detector) and appropriate electronics for data-processing.

A scheme of the components necessary for the Alpha-X technique is given in Fig. 3.10.

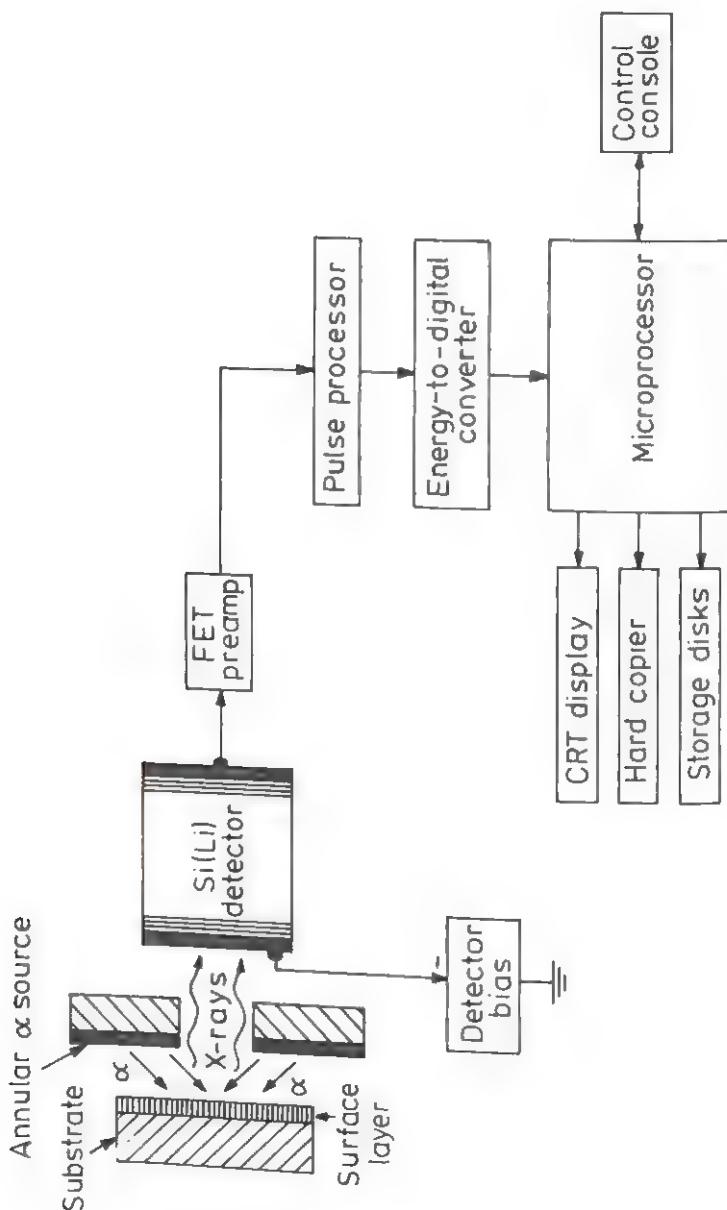


Fig. 3.10 Schematic diagram showing components needed for alpha-induced X-ray emission technique called Alpha-X [271] (by permission of the copyright holders, Technical Publishing Co., Barrington, U.S.A.).

The main advantages of Alpha-X over electron-excited X-ray techniques are (a) much better limits of detectability, because of the greatly reduced bremsstrahlung background radiation, and (b) direct correlation of X-ray data with elemental surface densities, e.g. film thicknesses. Layers between about 2 nm and several  $\mu\text{m}$  thick can be analysed quantitatively.

Expected areas of application include metallurgical processes (e.g. oxidation, corrosion, metal finishing, and friction and wear studies), thin-film processes (e.g. vapour-, sputter- and electro-deposition), fundamental and practical surface studies (e.g. catalysis), semiconductors (e.g. production control and failure analysis), and laser windows (e.g. coatings).

Although the Alpha-X technique does not have the very high surface sensitivity and micro-imaging capabilities of many of the other surface analysis techniques, e.g., Auger-electron spectroscopy, it provides a new and useful means for quantitative, non-destructive analysis of surface layers and thin films.

The equipment is suitable for complementary attachment to existing surface analysis systems such as AES or ESCA, providing very precise, non-destructive definition of layers with thicknesses up to  $10^4$  monolayers.

### *Synchrotron radiation*

Synchrotron radiation is the electromagnetic radiation from relativistic electrons moving in a curved trajectory. Because of its unusual properties, this radiation is very attractive for use in many exciting new experiments in which photons are used to probe the structure of matter, especially in the vacuum ultraviolet and X-ray regions of the spectrum. These are the spectral regions in which the photon wavelengths from a continuous source can be adjusted to match the characteristic wavelengths of atoms, molecules and solids.

Several properties of synchrotron radiation make it extremely useful for a variety of investigations. Among these is the continuous spectrum, with wavelengths ranging down to less than 1 Å in a 2.5-GeV electron storage ring.

The intensity of synchrotron radiation is far greater than that from the conventional vacuum ultraviolet and X-ray sources. Another very important property of synchrotron radiation is the virtually complete plane polarization of the radiation in the plane of the electron orbit. Another property of synchrotron radiation is the pulsed time-structure of the radiation, which makes many very interesting experiments possible.

Moreover, synchrotron radiation is extremely well collimated because of the way it is generated, so most of it can be collected and focused on the sample.

The intense continuous spectrum from a synchrotron radiation source extends from its high-energy limit (determined by the electron energy  $E$  and the magnetic field  $B$ ) through the visible and the infrared to the long-wave region. A tunable laser could also have all these properties, but tunable lasers will not give wavelengths much outside the visible region.

Recently, there have been a number of developments in the application of

synchrotron radiation, such as X-ray absorption experiments and angle-resolved electron photoemission [272].

Several investigations have now become possible because of the unusual properties of synchrotron radiation, although they have not yet been fully developed. For example, owing to the high collimation of the radiation, extremely small samples can be used, such as protein crystals. The pulsed nature of the radiation makes it possible to study time-dependent effects. Another promising area of research involves X-ray topography, an imaging technique based on the fact that strained and imperfect crystal regions diffract more strongly than perfect crystals. This makes it possible to study a wide range of defects in materials, including dislocations, voids, and grain structure in metals. Topographic techniques make it possible to observe magnetic domains through the distortion of the crystal lattice at domain boundaries, caused by magnetostriction.

There are many other possible applications of synchrotron radiation, such as small-angle scattering experiments on polymers and macromolecules, with monochromatic light at various wavelengths. There is also the possibility of nuclear fluorescence experiments which could yield information similar to that now obtained by Mossbauer spectroscopy.

Synchrotron radiation has advantageous properties for photoemission studies in general, and its array of available energies opens completely new avenues of surface analysis. The Stanford Synchrotron Radiation Project (SSRP) located at SPEAR (Stanford Positron Electron Accelerating Ring), started operation in 1974 as a facility open to users throughout the world for utilization of synchrotron radiation as an excitation source for research in physics, chemistry, biology and medicine.

#### *Proton microprobe*

The proton microprobe is the most recent technique in the field of non-destructive methods. It has been established that a combination of X-ray excitation by protons and detection of the emitted X-rays by an Si(Li) detector provides a powerful method for simultaneous non-destructive analysis for major and trace elements with atomic number  $\geq 12$ .

The research workers at Heidelberg [254], comparing the performance of the proton microprobe with that of other probes, especially the electron microprobe, find the following advantages and limitations of the technique.

The main advantage is that the sensitivity is one or two orders of magnitude better than that of the electron microprobe for detecting trace elements under normal operating conditions.

Most of the problems and limitations of the proton microprobe arise from the relatively large penetration depth ( $20\text{--}70 \mu\text{m}$ ) for protons with energies of  $0.5\text{--}4 \text{ MeV}$ , which has the following consequences.

(1) For very thin samples the sensitivity is reduced because of the enhanced background (bremsstrahlung and characteristic X-rays) from the sample support.

(ii) The X-ray yield changes with depth as the protons lose energy in the sample.

(iii) In fine-grained multicomponent targets there is also excitation of the areas just below the particle of interest, and this obscures the results. In addition, quantitative evaluation of the X-ray spectra is difficult because of X-ray self-absorption in the sample. Also additional background  $\gamma$ -rays produced by nuclear reactions might interfere with the characteristic X-rays.

To demonstrate the performance of the proton microprobe, it was used to determine the trace elements in some mineral grains in the lunar basalt (Apollo 17 sample 75015), the composition of which had previously been determined with the electron microprobe. Because of the sensitivity of the proton microprobe several elements were found in the sample that had been undetectable by the electron microprobe. For example, the spectrum of baddeleyite showed the presence of the K-lines of trace elements such as Ta, Pb, Th, W, Y, Nb, Ce, Pr and Nd, not detected with the electron microprobe. However, because of the intimate intergrowth with zirconolite grains, the spectrum could not be evaluated quantitatively.

In the geological sciences, especially petrology and geochemistry, the technique should allow determination of the partitioning of trace elements between co-existing minerals or phases in natural rocks and multicomponent synthetic materials.

We draw the conclusion that the experimental results obtained so far amply demonstrate the ability of the proton microprobe to show the presence of trace elements in solids at levels that cannot be detected, even qualitatively, with the electron microprobe.

The proton microprobe can also be used with good results in the analysis of aqueous biological samples.

Hercules [273] has discussed the present state of the chemical analysis of surfaces, one of the new frontiers in analytical chemistry.

#### 3.2.1.4 Kinetic and Enzymatic Methods of Analysis

Whereas with some analytical techniques (such as AAS and ASV, discussed above), there is the problem of finding adequate criteria for comparison of techniques which differ radically in principle, in the case of enzymatic and kinetic methods of analysis the problem does not arise, because the two techniques are basically similar. Indeed, many research workers regard the enzymatic methods as a special type of kinetic method, though this can be questioned from many points of view.

We consider that recent developments in the study of enzyme-catalysed reactions make the application of enzymatic methods a modern and independent domain of analytical chemistry.

As we shall see, according to their sensitivity and selectivity, kinetic and enzymatic methods are methods of trace analysis, sometimes competitive with radiochemical and radiometric methods of analysis.

As Guilbault remarked in the introduction of his book on enzymatic methods [274]: "The specificity of enzymes can solve the primary problem of most analytical chemists, the analysis of one substance in the presence of many similar compounds that interfere in the analysis. The sensitivity of enzymes allows the determination of as little as  $10^{-10}$  g of material".

Unfortunately, many analysts are unfamiliar with (or even ignorant of) these methods, which are less popular in industrial analytical control laboratories. A reason for this might be the high-school educational system, which pays little or no attention to modern analytical methods.

It was in the mid-1970s that reaction-rate methods became generally accepted and widely used on a routine basis. Two reference books were published in that period (by Yatsimirskii [275] and by Mark and Rechnitz [276]) which contributed to the introduction of this method into analytical laboratories. These books, besides the theoretical principles of the kinetic methods, gave a wide selection of reactions used for the determination of a large number of elements.

Interest in these methods grew substantially after the appearance of these books, a series of new methods being reported.

Of the reviews on kinetic methods, we mention those by Gary and Schwing [277] and by Weisz [278], which give a good account of the modern physical methods of analysis. Mark [279] has also written a useful article on the essentials of research on these methods.

Malmstadt *et al.* remarked [280]: "It is certainly not coincidence that the conversion from research interest to general routine use of reaction-rate methods corresponds to the development of a new generation of elegant, completely automated and computer-controlled chemical instrumentation".

Research in kinetic methods of analysis has followed four main lines.

- (a) The catalytic (or inhibitive) effect of the analyte on the reaction rate.
- (b) Detection of an equivalence point by catalytic effects.
- (c) Differential kinetics based on the difference between the reactivities of the constituents in a mixture towards a common reagent.

(d) Experimental techniques and processing of the results.

The kinetic methods have a high sensitivity, close to that of the enzymatic methods, but poorer selectivity. The competition between the two techniques since 1970 has favoured the enzymatic methods, as can be seen from the biennial review articles in *Analytical Chemistry*. This may be due to the increased availability of enzymes and their stabilization by different techniques, so that enzymatic analysis has become cheaper. It is sufficient to mention that the number of enzymes known by man has increased from fewer than 100 in 1930 to about 2000 today [281].

Another reason for the growth of interest in enzymatic analysis is the use, and recent introduction into many chemical laboratories, of enzymatic sensors.

Because the kinetic and enzymatic methods are typical trace methods, they have the operational disadvantages of interference from contamination. They

need reagents of high purity and appropriate laboratory equipment. They are useful, however, for control analysis of high-purity materials, biological and medical analysis, environmental control, etc.

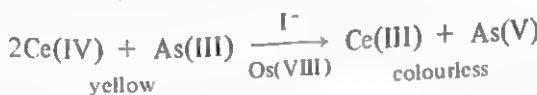
Because of the diversity of the publications on kinetic and enzymatic methods, we shall discuss here only a few aspects important for the future development of research in this field: (a) use of redox reactions as indicator reactions in kinetic methods; (b) immobilized enzymes; (c) enzyme electrodes.

### (a) Redox indicator reactions

An indicator reaction in kinetic analysis is the reaction catalysed by the substance to be determined. The most frequently used are redox reactions. The oxidation reagents used include  $H_2O_2$ , peroxoborate, oxygen, oxo-anions such as bromate, iodate, nitrate, peroxosulphate, periodate, and cations such as  $Ce^{4+}$ ,  $Fe^{3+}$ ,  $Ag^+$ . The reduction reagents include iodide, thiosulphate, arsenite,  $Sn^{2+}$ ,  $Fe^{2+}$ , organic dyestuffs such as alizarin, Malachite Green, Methyl Orange, and other organic compounds such as hydroquinone,  $\alpha$ -naphthylamine, *p*-phenetidine, *o*-tolidine.

The catalysts include copper, iron, manganese, titanium, zirconium, thorium, molybdenum, tungsten, osmium and ruthenium.

A versatile redox system used for kinetic determinations is that proposed by Sandell and Kolthoff [282] - the cerium(IV)-arsenic(III) reaction catalysed by iodide or osmium(VIII).



This reaction has found many applications, and can be monitored photometrically, potentiometrically [change of the ratio  $Ce(IV):Ce(III)$ ], biamperometrically and thermometrically.

The indicator reaction in the absence of the catalyst must be slow in comparison with the catalysed reaction. Yatsimirskii [283], by examining the mechanisms of redox reactions, has established some regularities which allow us to predict to a certain extent whether a redox reaction will be rapid or slow in the absence of catalyst.

The electron transfer between oxidant and reducing reagent generally takes place through an intermediate complex  $[Ox_1\dots Red_2]$  followed by another complex  $[Red_1\dots Ox_2]$  which decomposes, the sequence being as follows:



The existence, nature and formation constant of the first intermediate complex have been established in some cases [283]; for example, for the reaction

of  $\text{Fe}^{3+}$  with  $\text{S}_2\text{O}_3^{2-}$  the complex formed is  $[\text{Fe}^{3+}\dots\text{S}_2\text{O}_3^{2-}]$  ( $pK = 2.1$ ). The first intermediate complex may be a co-ordination or charge-transfer compound or an unstable ion-association species having a very short life.

According to Yatsimirskii [283], the speed of the reactions will depend on the types of orbitals involved in formation of the intermediate complex. Thus oxidants and reductants forming the complex by  $\pi$ -bonding between  $d$  orbitals will react rapidly, whereas  $\sigma$ -bonding involving  $s$  and  $p$  orbitals will generally result in slow reaction. It is difficult to say whether the rate of a reaction involving  $d$  together with  $s$  and/or  $p$  orbitals will be rapid, moderately slow, slow, or very slow. To give some examples, the oxidation of  $\text{Cr}^{2+}$ ,  $\text{Fe}^{2+}$ ,  $\text{Ti}^{3+}$  by  $\text{Mn}^{3+}$  is rapid, the oxidation of  $\text{Sn}^{2+}$ ,  $\text{I}^-$ ,  $\text{H}_2\text{AsO}_3^-$  by  $\text{ClO}_3^-$  is slow, but the  $d$ -type oxidant  $\text{MnO}_4^-$  oxidises  $\text{S}_2\text{O}_3^{2-}$  rapidly but  $\text{SO}_3^{2-}$  moderately fast and  $\text{H}_2\text{AsO}_3^-$  slowly (polyatomic  $s$ ,  $p$ -type reductants).

It is particularly important in kinetic methods to arrange that the reaction should be of first order with respect to the catalyst and a given reagent and of zero order towards all other species in the sample. The processing of the results is thereby considerably facilitated.

Table 3.13 gives some examples of elements determined catalytically by using redox reactions as indicator reactions, and shows the wide range of application.

Bontchev [284] has given a particularly useful exposition of the mechanism of catalytic reactions, and a discussion of the use of activators, which can increase the sensitivity by a factor of up to  $10^4$ , and also improve the selectivity.

Table 3.13  
Some examples of catalytic redox reactions [278]  
(by permission of the copyright holders, Verlag Chemie, Weinheim).

Substance	Reaction
Vanadium in blood	$p$ -Hydrazinobenzene sulphonic acid + $\text{ClO}_3^-$
Chromium	$o$ -Dianisidine + $\text{H}_2\text{O}_2$
Molybdenum in plants	$\text{I}^- + \text{H}_2\text{O}_2$
Manganese	Alizarin S + $\text{H}_2\text{O}_2$
Iron in plants	$p$ -Phenetidine + $\text{H}_2\text{O}_2$
Ruthenium in ores	$o$ -Dianisidine + $\text{IO}_4^-$
Osmium	$\alpha$ -Naphthylamine + $\text{NO}_3^-$
Ruthenium	
Osmium	
Cobalt in reactor cooling water	$\text{As}^{3+} + \text{BrO}_3^-$
Copper	Alizarin S + $\text{H}_2\text{O}_2$
	$\text{S}_2\text{O}_3^{2-} + \text{Fe}^{3+}$

**(b) Immobilized enzymes**

Enzyme immobilization goes back at least 60 years to the work of Nelson and Griffin [285], who adsorbed invertase on animal charcoal and observed that the adsorbed enzyme retained its biological activity and could be reused over a long period of time. However, these studies went largely unnoticed until Grubhofer and Schlecht [286, 287] immobilized several enzymes on polyaminopolystyrene and on Amberlite XE-64 resin by covalent attachment. At about this time other methods of enzyme immobilization also came into prominence.

Attachment to an inert support material can render enzymes insoluble, and the product can retain its catalytic activity. Once immobilized, an enzyme is often stable for weeks or even months. An obvious advantage of the immobilization is the ease with which the material can be separated for reuse. The support with its immobilized enzyme can simply be used in a batch-type process, with the analyte pumped off after the determination, or it can be packed in a column similar to those used in liquid chromatography and the sample solution passed through it.

A very interesting advantage of immobilized enzymes is the possibility of changing the chemical properties of the enzyme catalyst.

There are several methods of immobilizing enzymes such as absorption, adsorption, adsorption and cross-linking, ion-exchange, entrapment, copolymerization, covalent attachment. Of these, chemical attachment of enzymes to water-insoluble carriers is the most commonly used. Theoretically, covalent coupling offers the most stable and versatile method of immobilizing enzymes.

Figure 3.11 shows schematically the immobilization methods.

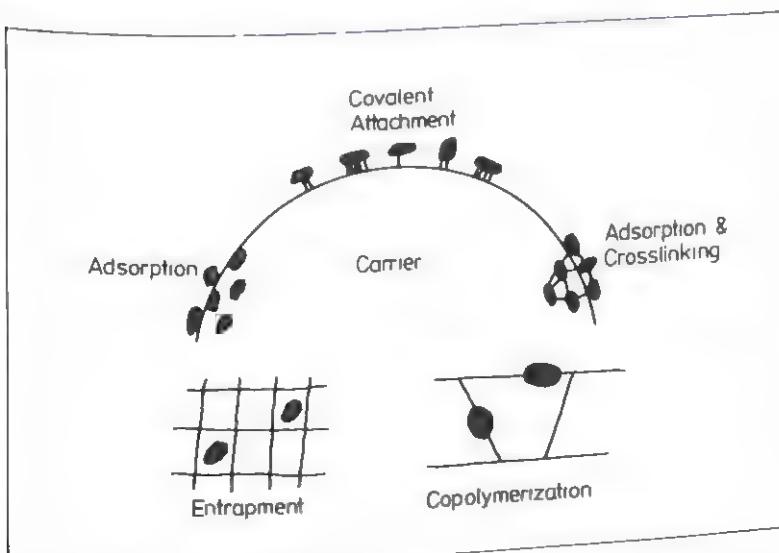


Fig. 3.11 - Methods of immobilization [281]. (Reprinted with permission from *Anal Chem.*, 1977, **49**, 1067A. Copyright by the American Chemical Society.)

Immobilization may cause several changes to occur in the apparent behaviour of the enzyme. It is well known that for each enzyme there is an optimal pH at which it shows a maximum reaction rate. When the enzyme is immobilized, the optimal pH may shift, depending on the nature of the carrier. Also when an enzyme is immobilized, an increase in  $K_m$  (the Michaelis constant) is generally observed. This increase is usually related to the charge on the substrate and/or carrier, diffusion effects, and in some cases, tertiary changes in the enzyme configuration. However, in some cases no change in  $K_m$  is observed.

Table 3.14 gives the  $K_m$  values for some soluble and immobilized enzymes.

**Table 3.14**  
Comparison of  $K_m$  values of some soluble and immobilized enzymes\* [288]  
(Reprinted with permission from *Anal. Chem.*, 1974, **46**, 602A.  
Copyright by the American Chemical Society.)

Enzyme	Substrate	$K_m$ , mM	
		Soluble	Immobilized
Invertase	Sucrose	0.448	0.448
Arylsulphatase	<i>p</i> -Nitrophenyl sulphate	1.85	1.57
Glucoamylase	Starch	1.22	0.30
Alkaline phosphatase	<i>p</i> -Nitrophenyl phosphate	0.10	2.90
Urease	Urea	10.0	7.60
Glucose oxidase	Glucose	7.70	6.80
L-Amino-acid oxidase	L-Leucine	1.00	4.00

\* All enzymes were immobilized on  $ZrO_2$ -coated controlled porous 96% silica glass particles.  $K_m$  values were determined under identical conditions for both soluble and immobilized derivatives for comparison.

Like all proteins, enzymes are susceptible to thermal denaturation, whether they are immobilized or in the 'free' state. In some cases the rate of inactivation and denaturation of an immobilized enzyme is lower than that of the free enzyme. However, enzymes which show excellent thermal stability do not necessarily show equally good operational stability, because the latter is a function not only of thermal stability but also of such factors as carrier durability, organic inhibitors, and concentration of inhibitors (including heavy metals).

Enzyme half-lives under controlled operating conditions should be temperature-dependent, but this does not mean that decrease in activity is a result of

Immobilized enzymes have found a series of applications in analytical chemistry. They also have important potential in biomedical applications. A very interesting book which discusses the biomedical applications, including ELISA (enzyme-linked immunosorbent assay) and EMIT (enzyme-multiplied immunoassay), has been published [289].

In the ELISA method, an enzyme is covalently linked to an antigen or antibody. The fraction not bound to a matrix-bound antibody or antigen is separated and assayed for enzyme activity.

The analytical and clinical applications of immobilized enzymes have been surveyed in an admirable book by Carr and Bowers [290], including the use of enzymatic electrodes, which will be discussed below.

First, however, we shall discuss the analytical application of immobilized enzyme columns. It is easy to immobilize several hundred units of active enzyme in a small (1 ml) column, thereby permitting equilibrium assays and eliminating many of the limitations of kinetic assay with soluble enzymes. For example, immobilized enzymes have been used in flow-through reactors of various configurations, including fixed-bed and open-tubular, as well as on electrodes and reagent pads.

Continuous-flow enzyme reactors have been used in clinical and environmental analysis. The combination of an enzymatic reaction and a non-selective detector is particularly attractive. We mention in this connection thermochemical immobilized-enzyme analysers. For example, the 'enzyme thermistor' has been applied to the determination of trypsin, glucose, lactose, uric acid, cholesterol, penicillin G, urea, etc., but a major drawback of many of these determinations has been the low sample throughput and large volume of sample required.

Schlifreen *et al.* eliminate these problems by using non-compressible porous glass supports and small, fast-response thermistors as heat sensors [291]. These authors made an investigation of the various mass- and heat-transfer processes involved in an immobilized enzyme enthalpimeter, to find how these factors can be adjusted to optimize system sensitivity, throughput and sample volume. The basic principles reported by them [291] are applicable to other enzymes and types of detector such as colorimeters and electrochemical transducers.

Owing to the numerous applications of immobilized enzymes various devices have been used in conjunction with enzyme reactors as the basis for specific analysers. For example, photometric flow systems using immobilized enzyme reactors have been developed for the determination of glucose, pyruvic acid, L-aspartic acid, penicillin G, urea, nitrate, phosphate, sulphate and uric acid.

Leon *et al.* [292] have described continuous-flow analysers in which glucose, glycerol and adenosine triphosphate were measured by the use of multiple enzyme tubular reactors. Martin *et al.* [293] have described a stopped-flow colorimetric analyser for glucose, and recently, Adams and Carr [294] have reported a coulometric flow-analyser for use with immobilized enzyme reactors.

The enzyme-substrate system chosen for this study was the urease-catalysed conversion of urea into ammonia and carbon dioxide.

(c) *Enzyme electrodes*

Ion-selective electrodes are the current fashion, largely because they can be successfully used for determination of organic, biological and biomedical compounds as well as inorganic ions.

The various types of ion-selective electrodes used in enzymology include conventional glass, homogeneous solid-state, liquid ion-exchanger, natural carrier-complex and gas-sensing electrodes.

The basic functional concept of the 'enzyme electrode' is the continuous instantaneous, electrochemical monitoring of enzyme-catalysed reactions, in which a substrate, coenzyme or inhibitor is converted by means of an enzyme into a product which may be measured by a conventional ion-selective electrode.

The first account of an enzyme electrode is probably that given by Clark and Lyons [295]. They determined glucose potentiometrically (and proposed that it could also be determined amperometrically) by means of immobilized glucose oxidase, according to the equation:



Updike and Hicks [296] introduced the term 'enzyme electrode' and made a dual cathode consisting of a Clark-type oxygen electrode with glucose oxidase immobilized in polyacrylamide gel. The electrode was used to determine glucose in whole blood and plasma, and thus demonstrated the feasibility of direct measurement on complex solutions.

The trapping of enzymes in a polyacrylamide gel has been successfully applied by several authors to the assay of urea, glucose, amino-acids, ethanol, etc.

Electrodes suitable for the rapid assay of D-phenylalanine, D-alanine, D-valine, D-methionine, D-leucine, D-isoleucine, D-norleucine and asparagine, based on the Beckman 39137 cation-selective electrode coated with the corresponding enzyme, are stable for up to one month [297].

Guilbault and co-workers [298-300] have coupled immobilized enzymes to electrochemical sensors to obtain analytical devices that incorporate the enzyme reagent and the sensor in the same unit. A number of these enzyme electrodes have been described, based on both ion-selective and gas-sensing probes.

An example of each type is shown in Fig. 3.12.

Immobilized urease is used for the measurement of the physiologically important substrate urea. It is worth mention that in 1963 Katz and Rechnitz [301] determined urea and urease after stoichiometric deamination, the final steady potential recorded with a Beckman univalent cation-selective electrode being proportional to the concentration of ammonium ions, and hence to half the urea concentration or urease activity.

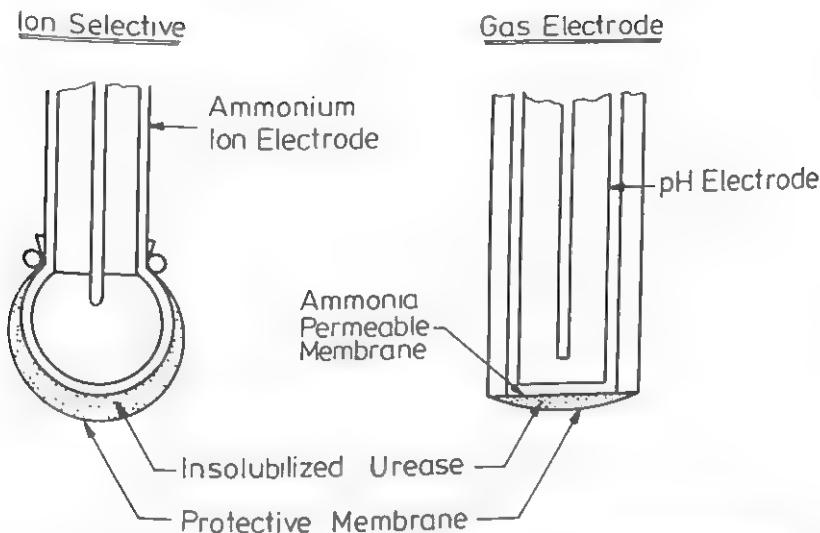
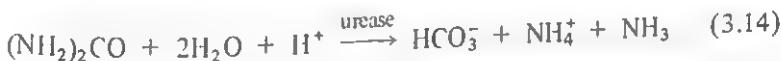


Fig. 3.12 Enzyme electrodes for measuring urea [281]. (Reprinted with permission from *Anal. Chem.*, 1977, 49, 1067A. Copyright by the American Chemical Society.)

Both methods shown in Fig. 3.12 rely upon the enzyme-catalysed hydrolysis of urea:



In the one case the urease is trapped in a gel matrix in direct contact with the glass surface of an ammonium ion-sensitive electrode. In the other, the immobilized urease contacts the hydrophobic gas-permeable membrane of an ammonia-sensitive electrode. Both electrodes function by diffusion of the urea substrate into the matrix of the immobilized urease, the products of the reaction ( $NH_4^+$  or  $NH_3$ ) affecting the sensor response in relation to their concentration. Unfortunately, because the ammonium-sensor responds to all univalent cations, including  $H^+$  (although there is some selectivity for  $NH_4^+$  relative to  $Na^+$  and  $K^+$ ), the high specificity offered by the enzyme is offset by the lack of specificity of the sensor. Even though the use of the ammonia gas-sensitive electrode eliminates this effect of interfering ions, there is still a limitation because the optimum pH for the ammonia gas-electrode is not the pH giving the highest activity of immobilized urease. For these reasons several instrument manufacturers have chosen to separate the enzyme and sensor functions to allow more latitude in the choice of conditions for both.

Table 3.15 lists the current commercial instruments using immobilized enzyme systems.

Of the review articles on enzyme electrodes, we recommend those by Gough and Andrade [302], Moody and Thomas [303] and Guilbault [304], as well as the biennial surveys in *Analytical Chemistry* (even-numbered years).

**Table 3.15**  
 Commercial instruments using immobilized enzymes [281].  
 (Reprinted with permission from *Anal. Chem.*, 1977, 49, 1067A.  
 Copyright by the American Chemical Society.)

Manufacturer	Analyte	Enzyme system
Leeds & Northrup	Glucose	Glucose oxidase
	Lactose	$\beta$ -Galactosidase + glucose oxidase
	Sucrose	Invertase + mutarotase + glucose oxidase
Yellow Springs Instrument Co.	Glucose	Glucose oxidase
	Galactose	Galactose oxidase
	Cholesterol (announced)	Cholesterol oxidase + cholesterol esterase
Technicon Corp.	Glucose	Hexokinase + glucose-6-phosphate dehydrogenase
Midwest Research Institute	Insecticides	Cholinesterase
Owens-Illinois (Kimble Division)	BUN	Urease
	Glucose (announced)	Glucose oxidase

The combination of an enzyme with an ion-selective electrode gives a very sensitive and selective technique, suitable for use in automated on-line analysis. The selectivity can be greatly increased by using two immobilized enzymes with the electrode [305, 306]: the first enzyme reacts with the analyte to produce the substrate for the second enzyme, which in turn produces the species to which the electrode responds. Such electrodes can be especially useful in the food industry or wherever carbohydrates are used, since there are many specific enzymes for carbohydrates, and at least 50 which catalyse oxidation of substrates with consumption of oxygen, providing numerous possibilities for exploitation of oxygen-sensitive electrodes.

### 3.2.2 Structural Analysis

There is no doubt that the most spectacular and difficult domain of analytical chemistry is that of structural analysis. With a few exceptions, analytical teaching in this field is unfortunately deficient, analytical courses usually giving less theoretical and practical instruction than their inorganic, physical and organic counterparts. This is probably because analytical chemists have hitherto been concerned essentially with the composition of a substance, its structure being determined by other specialists. This has led in some cases to erroneous structures

being proposed for complex compounds on the basis of only the analytically determined stoichiometric ratio.

There are now many techniques which can be used in conjunction to establish the structure of inorganic, organic or organo-metallic compounds. We shall discuss some of them (and their performances) here, dividing them into three main groups: infrared spectrometry-Raman spectrometry, mass spectrometry-nuclear magnetic resonance spectrometry, and X-ray diffraction-neutron diffraction.

### *3.2.2.1 Infrared (IR) Spectrometry-Raman Spectrometry (RS)*

These two techniques are complementary, since Raman observations are possible on infrared-inactive vibrations and vice versa.

Until recently, Raman spectroscopy was considered to be limited by the sources available. Even with high-intensity mercury discharge lamps, measurements were made with difficulty. The advent of lasers has dramatically altered this situation and significantly improved the growth potential of the technique [307].

The number of publications on IR spectrometry is considerably greater than that on Raman spectrometry. As an example, the full CAC (Chemical Abstracts Condensates) data-base for 1976-77 contains about  $8 \times 10^5$  citations, the total number of citations pertinent to IR spectrometry being about 8200, approximately 1% of the whole [308], but of these only a fraction refer to Raman spectrometry.

The introduction of Fourier transform (FT) methods has had an effect on IR spectroscopy comparable to the renaissance, mentioned above, that occurred in Raman spectroscopy with the development of continuous-wave gas lasers.

We shall therefore discuss in the following only these modern aspects of the IR and Raman techniques in order to show that apparently obsolescent analytical methods can enjoy a second youth if their operational parameters are improved.

#### *Fourier transform infrared spectroscopy (FTIR)*

The Fourier transform is basic to the very nature of a spectroscopic measurement since the dispersion step is, in effect, a Fourier transformation of the electromagnetic signal. The Fourier transform is intimately related to instrumental measurements through the convolution integral, and the important topic of spectral resolution falls in this area [309].

Both for FTIR and FTNMR the measurement step results in the recording of a signal that is the Fourier transform of the conventional spectrum. It is evident that analytical chemists need a basic understanding of the Fourier transformation. We shall discuss in the following some aspects of this technique, based on review articles [309, 310].

In brief, to measure a spectrum with an FT spectrometer, a Michelson interferometer is illuminated with a source of 'white' or polychromatic radiation

and the movable mirror is translated over a distance (from  $-L$  to  $L$ ) which depends on the desired resolution. The output signal is passed through a sample (or the sample itself serves as the source), and the resulting interferogram signal is received by an IR detector.

The difference in principle of operation between an FT spectrometer and a conventional grating instrument results in two major advantages of FT spectroscopy. These are Fellgett's (or multiplex) advantage and Jacquinot's (or throughput) advantage.

Suppose that the spectrum of interest lies between  $\nu_2$  and  $\nu_1$ . Then the number of spectral elements,  $n$ , is defined by  $n = (\nu_2 - \nu_1)/\Delta\nu$  where  $\Delta\nu$  is the band-width accepted by the detector. Thus, a spectral element is that part of the signal  $S(\nu)$  between  $\nu_2$  and  $\nu_1$  which is seen by the detector at any given time. If  $t_G$  is the time required to measure a single spectral element, then  $nt_G$  is the total time required to scan between  $\nu_2$  and  $\nu_1$ .

An FT spectrometer contains no dispersing element or slit, and therefore all of the spectral information contained in the interval  $(\nu_2 - \nu_1)$  is received by the detector in the time  $t_{FT}$  required to record the interferogram.

If it is assumed that the response times of grating and FT spectrometers are the same,  $t_G = t_{FT}$ , then the spectrum can be recorded  $n$  times faster with the FT spectrometer than with the grating instrument, with the same signal-to-noise ratio ( $S/N$ ).

If the same total time,  $nt_G$ , is taken by the FT spectrometer to record the spectrum, then the gain in  $S/N$  is given by:

$$\frac{(S/N)_{FT}}{(S/N)_G} = \left( \frac{nt_G}{t_{FT}} \right)^{\frac{1}{2}} = n^{\frac{1}{2}} \quad (3.15)$$

The gain of  $n^{\frac{1}{2}}$  in  $S/N$  is known as Fellgett's advantage or, more descriptively, as the multiplex advantage. If  $t_G = t_{FT}$  the FT spectrometer examines the entire spectrum in the same period of time that the grating instrument requires to examine a single spectral element.

Jacquinot's (throughput) advantage results from the loss in energy of the input source in a dispersive instrument because of the presence of a grating and slit between the source and the detector. Such losses do not occur in an FT spectrometer because these components are not required.

The ratio of the energy throughputs ( $E$ ) for an FT and a grating instrument is given approximately by  $E_{FT}/E_G \sim 2\pi(F/l)$ , where  $F$  is the focal length of the collimator and  $l$  is the slit-height. This expression assumes that the grating in the dispersive instrument is set at the angle of maximum efficiency.

The high throughput of interferometric spectrometers means that they can be used to great advantage in observing spectra from very weak sources.

Two types of FTIR systems are currently used, based on either slow- or rapid-scan Michelson interferometers. For spectroscopists the rapid-scan systems

are of most interest. Such systems may be used to study the spectra of transient chemical-reaction species with half-lives of the order of seconds.

Other interesting applications of rapid-scan FTIR systems, thanks to the good *S/N* ratio and small energy losses, are to obtain spectra of short-lived species and to make determinations in the presence of a strongly absorbing solvent (aqueous solution).

A new technique, with good performance, is the application of rapid-scan FTIR systems in combination with gas chromatography, for the study of complex mixtures. FTIR spectra also have great potential in surface studies [311]. The high signal-to-noise ratio of the spectrum, combined with digital processing of the spectrum by computer, makes FTIR very attractive for surface studies.

IR spectra of good quality can be obtained from 0.5- $\mu\text{g}$  quantities of transient species in the gas phase by means of rapid-scan FT spectroscopy [310].

We have described above, very briefly, the principles and some applications of a technique of the future. This technique is at present expensive, but we hope that its performance will lead to its being fully exploited in the structural study of chemical compounds. A good description of this technique may be found in Griffiths' book [312].

### *Laser Raman spectroscopy*

As we have mentioned, the use of the laser has revolutionized Raman spectroscopy and made it as versatile a technique as its absorption counterpart.

The Raman range covers the same region as the middle-to-far IR, falling between the visible and microwave regions. In 1923 Smekal [313] predicted the existence of this light-scattering phenomenon, which was demonstrated by Raman [314] in 1928 and is named after him.

It differs from the radiation-scattering effects of particles (Tyndall effect) and molecules (Rayleigh effect). Raman spectra are observed when visible light is scattered inelastically by molecules in solids, gases or liquids.

Raman effects are relatively inefficient processes; about 0.1% of the incident radiation intensity appears as Rayleigh scattering and approximately  $10^{-4}\%$  as Raman scattering.

Raman scattering can result from rotational, vibrational or even electronic transitions. Because the Raman effect is weak, it is desirable that the material should scatter the radiation rather than absorb it, therefore coloured species are difficult to study. Even weak fluorescence is much stronger than the Raman effect, and therefore it is difficult, for example, to study rare-earth and many organic compounds. Another difficulty is that turbidity or even dust particles will increase the intensity of the Rayleigh-scattering line relative to the Raman lines, with undesirable consequences. Other disadvantages of this technique which earlier made it of limited application were eliminated when the laser was introduced as a source in the early 1960s. Light produced from a non-laser

source is emitted from many points independently so that there is no phase relationship, directionality, and polarization of the radiation.

The laser is an almost ideal light-source, and hence laser Raman spectroscopy has become a method of analysis that is as easy to use as infrared and ultraviolet absorption spectroscopy.

The introduction of the laser as light-source has eliminated a series of disadvantages of mercury-arc excitation. Some of the advantages of the laser as a light-source are that most fluorescence problems are eliminated; the collimated nature of the laser energy allows focusing for excitation of extremely small volumes, and the laser's high intensity and nearly completely linear polarization simplify the measurement of depolarization values.

The most commonly used laser is the helium-neon source emitting at 632.8 nm (red). The argon-ion laser has also found some application with its emission at 488.0 nm (blue-green) and 514.5 nm (green). The laser beam has a very narrow spectral line-width (0.005 nm for a helium-neon laser, compared with 0.025 nm for a mercury arc). The nature of the laser cavity results in an automatically-collimated intense light-beam, giving very high illuminating efficiency. An effective luminous flux of several hundred  $\text{W/cm}^2$  can be achieved with a relatively low-power laser.

In contrast to the lasers mentioned above which emit discrete lines, tunable dye lasers find general use as Raman sources. Two techniques based on these sources have appeared, namely coherent anti-Stokes Raman spectroscopy (CARS) and resonance Raman spectroscopy. Both depend heavily on the tunability of the excitation source [315].

Figure 3.13 gives the scheme of a laser Raman spectrometer.

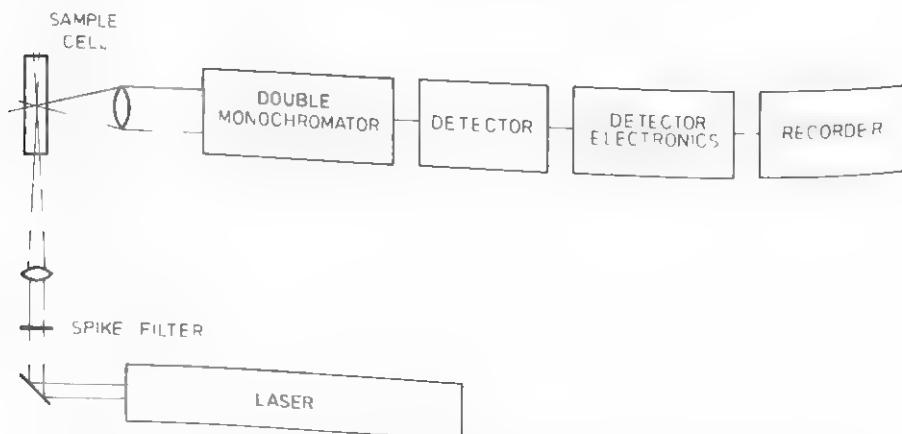


Fig. 3.13 Schematic of a laser Raman spectrometer [316] (by permission of the copyright holders, J. Wiley Inc., New York).

Commercial spectrometers are equipped with double or triple monochromators that effectively eliminate stray light, but for chemical studies a double monochromator is satisfactory. The Raman band frequencies should be accurate and reproducible to within  $\pm 2 \text{ cm}^{-1}$ .

The applications of laser Raman spectroscopy are extremely numerous and cover inorganic, organic and organometallic compounds. In the past Raman spectroscopy was applied only to a number of colourless inorganic or organic compounds.

The first report of the Raman spectrum of a coloured organic material appeared as early as 1964, and the first laser Raman results of direct interest to chemists were obtained in 1966; the yellow cation  $[\text{Co}(\text{NH}_3)_6]^{3+}$  was examined in solution, and the deeply coloured anions  $\text{MX}_4^-$  [M being platinum, palladium or gold, and X chlorine, bromine or iodine; the compound potassium tetrailodoaurate(III) ( $\text{KAuI}_4$ ) is soot-black in bulk] were examined as powders.

Although the first Raman spectrum of a polymer (polystyrene) was obtained in 1932, laser Raman spectra of polymers were not readily available until recently. The first high-quality spectrum (of isotactic polypropylene) was produced in 1967, shortly after the introduction of the laser source, and in the past few years there have been numerous publications describing the applications of Raman spectroscopy in the synthetic polymer field.

A series of applications of this technique may be found in review articles and books, of which we mention two [316, 317].

To end this section we stress the difficulty for the analyst to choose the most appropriate method to establish the structure of a chemical compound. This difficulty may be caused by inadequate knowledge of the method or by preconceived ideas. The analytical chemist must be fully aware of the up-to-date performance of the different methods of structural analysis, in order to make the best choice, particularly when complementary techniques (such as IR and Raman spectroscopy) are available.

### 3.2.2.2 Mass Spectrometry (MS)-Nuclear Magnetic Resonance Spectrometry (NMR)

Owing to the wide area of application of these techniques we shall discuss only some special aspects in order to demonstrate their importance for chemical analysis.

#### *Mass spectrometry (MS)*

This technique had its origins at the beginning of this century, in Thompson's studies which gave conclusive evidence of the existence of isotopes. MS has nowadays become a widely used technique for research, owing to the continued improvement of the equipment and to the appearance of new working methods.

Mass spectrometry was first used only for the study of isotopes. After the second world war it was applied to the structural study of organic compounds.

Most recently, spark-source mass spectrometry has proved its utility in the determination of elements present as traces in inorganic substances, high-purity materials, semiconductors, etc., allowing the determination of elements at the ng/g level. However, the most spectacular application remains the structural analysis of organic compounds. McLafferty observed in the introduction of the Romanian book by Oprean [318] "There is a feature of mass spectrometry which according to my opinion remained unchanged during the time. ... This is the challenge, the stimulus and the amusement characteristic of mass spectrometry, similar to a game of crosswords, and namely to obtain an eloquent picture of a molecule from different detected fragments".

The great value of research in the field of MS and especially use of the mass spectrometer as a detector in the combined GC/MS technique has been proved in the Viking Lander missions to Mars. In an article [319] on the search for organic and volatile inorganic compounds in two surface samples from the Chryse Planitia Region of Mars, it was reported that the existence of organic compounds on Mars was highly improbable, only CO<sub>2</sub> and water being detected by the automated GC/MS analysis of Martian soil. The samples were heated at 200°, 350° and 500°C to expel volatile substances and pyrolysis products which were then analysed by GC/MS. The material released only 0.1–1% of water when heated to 350° or 500°C. This water was presumably present in mineral hydrates which release water at these high temperatures. The samples did not contain organic compounds more complex than, for example, propane or methanol, at a level of 1 part in 10<sup>9</sup>. Low molecular-weight compounds of this nature were not present at levels above 10 ppm (the detection limit used).

These results seem to exclude the existence of any efficient contemporary process that produces organic compounds. It also makes it unlikely that there are low-efficiency processes occurring over a long period and causing accumulation of organic compounds stable in the Martian environment.

The fields of application of MS include biomedicine, environmental studies, toxicology, entomology, geochemistry, biochemistry and organic, organo-metallic and inorganic chemistry.

As Burlingame *et al.* have remarked [320]: "This impressive range of interest in mass spectrometry, therefore, requires a variety of inlet systems, ion-source types, mass analysers, mass ranges, mass resolutions and data systems. It is this proliferation of techniques that has led to the situation where it is not always easy to select the most appropriate method(s) from the sometimes exaggerated claims in the literature and from instrument companies".

If mass spectrometry is compared with other techniques of structural analysis, its sensitivity is higher than that of NMR or FTIR, despite the application of Fourier transform techniques to enhance the data in these two areas. It is possible on some instruments to obtain full mass spectra on 1 ng of material in about a second. We may note the remarkable rapidity with which analytical information is obtained. If this technique is coupled with GC, mixtures of

different compounds of various molecular weights or complexity may be analysed.

A further advantage of mass spectra is their suitability for data storage and library retrieval.

The greatest disadvantage of MS relative to IR, Raman, X-ray diffraction and neutron diffraction is that it is a destructive technique.

We shall now examine a technique which can serve as an alternative to GC/MS for some types of problem, namely a direct technique of analysis of mixtures by mass spectrometry, by a non-chromatographic procedure. It is called MIKES (mass-analysed ion-kinetic energy spectrometry). The MIKES approach to mixture analysis is generally applicable and has advantages over other currently used methods. In this non-chromatographic procedure the mixture of components is separated after rather than before ionization. An analogy can be made between this procedure and fluorescence spectroscopy (Fig. 3.14).

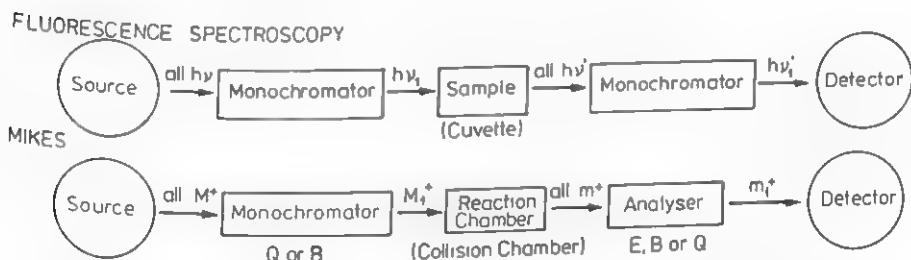


Fig. 3.14 Scheme of mixture analysis by MIKES as compared with similar steps involved in fluorescence spectroscopy. E, electric sector; B, magnetic sector; Q, quadrupole mass analyser [321]. (Reprinted with permission from *Anal. Chem.*, 1978, 50, 81A. Copyright by the American Chemical Society.)

As can be seen from Fig. 3.14 the ionized mixture is passed through a monochromator (which may be operated as a momentum or mass analyser), and the selected component is dissociated without appreciable change in velocity. The product ions are then analysed and detected. The second analyser can be operated as a mass, momentum or kinetic-energy analyser since for constant velocity, the mass, momentum, and kinetic energy are directly proportional to each other [321].

MIKES may be used to determine the components of complex mixtures, including biological tissue, without any prior chemical separation whatsoever. Barbiturates have been examined by the MIKES method with good results, whereas GC/MS does not give good results in this case. This technique holds considerable promise for application in biochemistry, and its detection limit is better than that of mass spectrometry.

It is obvious that direct analysis of mixtures by MIKES can serve as an alternative to GC/MS. Moreover, the sample throughput capabilities of MIKES

are expected to be greater than those for GC/MS for those analyses that are not signal-limited.

Table 3.16 gives some of the features of MIKES and GC/MS.

There is no doubt that the continued development and automation of this technique will make it competitive with the best techniques of structural analysis.

**Table 3.16**

Comparison of selected characteristics of MIKES and GC/MS methodologies [321]

(Reprinted with permission from *Anal. Chem.*, 1978, **50**, 81A.

Copyright by the American Chemical Society)

	MIKES	GC/MS
Thermal stability	Moderate	Severe
Analysis time	Short	Long
Exposure to extraneous material	Minimal	Severe
Detection limit	$10^{-9}$ - $10^{-10}$ g	$10^{-11}$ - $10^{-12}$ g (SIMS)
Quantitation	Yes	Yes

#### *Nuclear magnetic resonance spectrometry*

NMR is based on Gartner's theoretical studies (1936) and was experimentally founded independently in 1945 by Bloch's team (Stanford University) and Purcell's team (Harvard University).

Its importance for structural analysis was soon recognized, and the two physicists were later awarded the Nobel prize. Twelve years later saw the establishment of  $^{13}\text{C}$ -NMR.

The development of superconducting solenoids, together with Fourier transform techniques, has made observations of spectra of low-abundance and/or low-sensitivity nuclei a routine matter (the abundance of  $^{13}\text{C}$  is only 1.1%), and the wealth of information on molecular conformation, dynamics, etc., available from these spectra is enormous. The equipment for NMR becomes continuously more sophisticated and now offers information about atomic species such as phosphorus, fluorine, boron, etc.

For the study of organic compounds, the most suitable methods are proton or  $^{13}\text{C}$ -NMR. An interesting comparison of both techniques may be found in Silberg's book [322].

High-resolution NMR spectra obtained from liquid samples are routinely employed in structural determination and in the examination of chemical dynamics in solution.

The observation of chemical shift, quadrupole and dipole tensors in solids can also provide structural data, and when molecular motion is present in a

solid sample, the spectra can in principle elucidate the rate and mechanism of that motion [323].

The theoretical and practical aspects of NMR are various. We shall discuss only some features of dynamic nuclear magnetic resonance spectroscopy. This technique became possible as a consequence of the recent development of the equipment for the measurement and interpretation of NMR spectra which would allow determinations in very short time-spans at temperatures down to 77 K. A very good book on this area has recently been published [324].

It is well known that the spectrometric methods used for studying dynamic processes have to be chosen according to the energy involved. In the case of electronic spectroscopy, the energy needed for a transition is of the order of several hundred or more kcal/mole; in IR the energy of a transition is some 1-10 kcal/mole; in NMR a difference of 100 Hz (at 60 MHz) is equivalent to about  $10^{-7}$  cal/mole.

The difference is fundamental and has an implication for the 'time scale' through the lifetime of the excited state. According to the Heisenberg uncertainty principle, there is a connection between the time parameters and the width of the spectral line or the NMR signal. The relationship between the lifetime of the spin in a given state and the width of the signal allows two states of closely similar energy to be differentiated.

An essential factor in the time-dependent processes is that if a nucleus changes its magnetic environment because of a given chemical process, two limiting cases may be distinguished [322].

(i) The change is slow on the NMR time scale; in this case the two states of the nucleus are separately observed as signals of two distinct species. This is useful for conformational analysis.

(ii) The change is very rapid in both directions; in this case the average of the spectral parameters (chemical shift, coupling and time of relaxation) of the two states of a nucleus is observed.

The rates readily measurable by magnetic resonance techniques extend from about 1 to  $10^6$  sec $^{-1}$ , a very wide and important range that is too fast for many of the more conventional approaches.

This technique, owing to its particularly high performance and to the improvement of the equipment and the theoretical studies, is currently extensively used in research on problems such as cycle inversion, conformational equilibria in acyclic systems, configurational inversion, proton transfer, hydride ions, valency tautomerism, etc.

If we read Jackman and Cotton's book [324] we see that the applications of this technique are numerous, some of them exotic or even impossible to solve by other techniques. For example, the stereochemical non-rigidity in metal carbonyl compounds, a very intricate problem of structural analysis, and stereochemical non-rigidity in organo-metallic compounds have been studied by use of this technique. (The term 'stereochemically non-rigid' is used for all molecules that

undergo intramolecular rearrangements rapidly enough to influence NMR line shapes at temperatures within the practical range of experimentation.) The equipment necessary for this technique is unfortunately too expensive to be accessible for students. The graduate students must learn only how this technique should be used and correlated with other results from IR, MS or Raman spectrometry studies.

Unfortunately, NMR suffers from a series of disadvantages, difficult to eliminate. Each spectrum represents a separate problem in interpretation. Proton-NMR requires deuterated solvents which are expensive, and  $^{13}\text{C}$ -NMR needs costly and complex apparatus, is suitable only for research purposes, and is not in itself useful in education, especially in the 'poor' universities.

### 3.2.2.3 X-Ray Diffraction–Neutron Diffraction

These two techniques of structural analysis will be discussed together because they have identical physical principles and complement each other in the information that can be obtained with them. There are many books, review articles and publications in this field, but few of them discuss comparatively the performances and theoretical aspects of these methods, an exception being the book by Bally *et al.* [325].

Although X-ray diffraction, thanks to automation, is now accessible to most chemists, neutron diffraction still remains unpopular because of the complexity of the experimental work. However, modern reactors provide beams of thermal neutrons sufficiently intense to serve for study of the microstructure and microdimensions of substances.

The coherent scattering of X-rays by an isolated atom is determined by the interactions of the incident radiation with the electrons of the atom. Neutrons may be scattered by an atom by two types of interaction: between the neutron and the atomic nucleus, and between the intrinsic magnetic moments of the neutron and of an atom having partially filled electronic shells.

The detectors used in X-ray diffraction include photographic film, and ionization or scintillation detectors; for neutron diffraction proportional detectors and scintillation detectors are used. The proportional detectors use boron trifluoride as filler gas; the scintillation detectors contain a two-component mixture, the first component giving nuclear reactions with neutrons to produce ionized particles which cause scintillation in the second component of the mixture. The first component is usually a compound of boron or lithium. The second determines the physical state of the detector (plastic, vitreous, liquid).

The optical scheme for neutron diffraction requires the beam incident on the sample to be monochromatic and plane-parallel, this being achieved with a crystal monochromator. The diffraction maxima are recorded by means of the detector (usually a proportional counter) which rotates around the sample together with a collimator which sets the limits of the 'observable' angle. To achieve this experimentally, three collimators with plane-parallel slits (Soller

type) are used, the first before the crystal monochromator, the second between the crystal and sample and the third between the sample and detector.

The purpose of qualitative and quantitative structural analysis of crystalline powders is to establish the components and their proportions in a sample. In qualitative structural analysis the diffraction data for the sample are compared with those catalogued for known crystalline substances (in the ASTM index, which systematizes the structural data obtained with diffraction studies).

The integrated intensity of a diffraction maximum for a given structural component will be proportional to the volume fraction occupied by this component. This property of the integrated intensities may be used for quantitative structural analyses, to establish the concentrations of different structural components.

An interesting application of neutron diffraction is the structural analysis of magnetic substances.

The X-ray diffraction technique is used for gases, liquids and amorphous solids as well as for crystalline materials. These other types of material have a statistically isotropic structure. This means that the function for the probability density,  $P(r)$ , of scattering matter in a spherical shell of radii  $r$  and  $r + dr$  is expressed in terms of a density function,  $\rho(r)$ , representing the average number of atoms in the shell, and  $\rho_0$ , the average atomic density of the system.

$$P(r) = \rho(r)/\rho_0 \quad (3.16)$$

This property of isotropy of atomic environments has only a statistical character. It assumes the existence of a local anisotropic environment having different symmetries which correspond to the nature of the chemical bonds or to the necessity of spatial packing. For use with amorphous substances the X-ray diffraction method needs well-stabilized sources and emission tubes of high power (for example 2 kW). However it allows direct recording of the diffracted radiation, and as absorption by the sample is practically independent of the diffraction angle  $2\theta$ , no absorption correction is necessary. The main advantages are the high sensitivity and precision achieved in measurement of the diffracted intensity (owing to the relatively large amount of irradiated material, which results in good statistics in the detection counter system).

The X-ray diffraction techniques have been successfully used to characterize the structure of polymers, biopolymers, nucleic acids, proteins, etc.

As a result of its complete automation and the improvements in equipment, X-ray diffraction has also embarked on a second youth, being one of the basic techniques of structural analysis, giving direct knowledge of the structure.

At the symposium on 'Instruments for Tomorrow's Crystallography' held at the winter meeting of the American Crystallographic Association, 19-23 January 1976, three very promising directions for improving X-ray diffraction instrumentation were outlined:

- (1) the use of synchrotron radiation;

- (2) energy-dispersive diffractometry with solid-state detectors;
- (3) the utilization of position-sensitive radiation detectors in X-ray diffraction instrumentation [326].

Although the interpretation of diffraction spectra needs knowledge and experience, its principles should be known by the modern analytical chemist.

### 3.3 OUTPUT

*Where there's a will there's a way.*

This attempt to present aspects of teaching and education in analytical chemistry is approaching its end. We call it an attempt since it is close to impossible to give general advice on education and teaching, even in a specialized field such as analytical chemistry. However, in this comparatively small number of pages we have kept to the general aspects which we consider most relevant to education and teaching in this discipline, which is so useful today to all chemists and to a large number of other specialists.

The sequence of presentation was deliberately arranged to be congruent with the sequence of steps in an analysis, so the sections in Chapters 2 and 3 'correspond'.

Information-Input, Experimental-Black-Box, Data Processing-Output.

It should be stressed, however, that the titles of sections in Chapter 3 are intended only to be thought-provoking and not to refer to the steps of automation in and through analytical chemistry.

In the earlier sections we have made extensive use of information available in the literature as well as expressing our own opinions, but now, we wish to give only our own thoughts. We therefore make a *tabula rasa* of knowledge acquired from the literature and put to work our experience of 25 years in research and teaching, in order to emphasise some aspects of the teaching of analytical chemistry, and its efficiency.

Since throughout this book we have been drawing conclusions by contrasting man and instrument, this section is divided into two parts: one is going to deal with the quality of the analyst, and the other with the quality of the analytical signal. We think this division is logical since any product is evaluated in terms of its quality and the product of thought is no exception.

#### 3.3.1 Quality of the Analyst – the Three 'C's

Discussing the qualities that education and teaching can inject into an analyst is a highly subjective venture. Here we discuss only three facets of an analyst, which must characterize any specialist, no matter what the nature of the specialization.

(a) *Capability.* We start with this 'C' since it is a *sine qua non* for any person with a level of education equivalent to at least that of a bachelor of science.

Being capable means having understood the 'job', and being able to adapt to the work in the particular field. Changes in the educational system (in chemical education these changes are useful if properly directed but can be disastrous if not) are, however, unfortunately accompanied by fluctuations of the quality of the educational product, so capability is likely to vary from time to time and from institute to institute.

As we have already said, teaching only opens the ways to education and if the connection does not work smoothly, flaws develop in the quality of students, especially in their capability.

To be a good analyst, it is necessary first to have a general culture, then a general chemical culture, and plenty of patience to improve them continuously. The professor with whom the student interacts every day has the major role as character builder. The beginners imitate, and imitation of those professors who are distinguished by capability is very much to the beginners' profit.

Being capable means before anything else being keen to understand all the subtleties of the profession chosen.

All of us recall with great pleasure those of our professors who delivered their courses in such a way that the audience was fascinated. Such an 'attractive' course can be offered only by highly cultured persons. Course presentation must be enlivened and broadened with collateral remarks regarding other fields of activity, remarks which force the audience to establish connections for themselves.

Very often, the beginners who sit in a good class become enthusiastic and, as we said above, feel like imitating their teacher; this will encourage them to enlarge their knowledge and will send them to the 'church' of any scientist – the library.

Only attending a good class will produce this 'active' impulse to use the library; a second-rate course is apt to produce displeasure with the whole field, and at best produces a 'passive' desire to use the library – in self-defence!

Cases are not infrequent of freshmen who intend to specialize in a certain field but dramatically decide to change it after taking a brilliant course (in a different field) which highly impresses them.

The library is the nursery where capable people are bred, and the shrine where they learn to think, to analyse the ideas of others and shape their own ideas. Library work is the vital route to expertise in gathering, assessing, interpreting and using information, and must not be discontinued or become mere routine. Though specialists needing to solve some problems rapidly may resort to the computer to get the information needed, the beginner should, in our opinion, scan the journals directly, and definitely avoid making use of computerized 'rapid' information. We would even go further and say that the specialist should also restrict his computer searches to occasions of dire necessity.

We favour the idea that study in the library plays a formative part, and that like many sports, this kind of activity has no age limit. Those who are frequent visitors to libraries are impressed by seeing celebrated scientists reading and

thinking creatively next to them; in spite of their achievements these scholars are still willing to learn and continue their education, to promote productivity.

Regular use of the library ensures exercise of the mind just as daily training keeps a sportsman in shape. If this exercise is done properly it contributes to the development of capability.

Old specialists are considered by many to be less productive than young ones, and 'limited' in outlook and ability. We think this is not so. Let us not forget that Goethe was old when he wrote Faust, the masterpiece of his creative life, and that Faust has been read with pleasure by a great many people; we are sure it will be enjoyed just as much by future generations.

We consider that 'limitation' can be cured in the library; the library is a palliative for all except those who cannot read between the lines. It is a refresher for capable people willing to make use of it and to try to develop their intellect.

We have insisted so much on work in the library because only continuous study allows us to discover the imperfections of our own culture, the more so as while reading we get new ideas and so approach new lines of research.

Any one of us who has been working for several years in a certain field may suddenly feel that his efficiency has dropped below its usual standard; otherwise capable people are therefore very often convinced by their common sense that they have grown limited. The library is the right cure at the right time. We all have a rough idea from the literature of what is going on in chemistry in general and realize that from time to time 'fashionable' fields of research arise (their exponents call them priority fields) and that there is a rush to be 'in the swim'. Just now, if we make a comparative statistical study of quantitative analytical chemistry, we conclude that such fields as HPLC, ion-selective electrodes, and analysis of surfaces are among the priority fields. Usually such fields are indeed highly important, but occasionally the fashion proves a false one and is short-lived.

The development of such fields is discovered in the library and is followed the world over by explosions of interest and of work in those particular fields. Thus both theoretical and practical information accumulates very rapidly. Perhaps the best examples of this kind of dynamic growth are atomic-absorption and nuclear magnetic resonance which shortly after their birth 'marked an epoch' and have cured many analysts of 'limitation', or even rejuvenated them.

For maintenance of capability it is vital to preserve freshness of thinking. This is not achieved by drugs, but by approaching from time to time one of the priority fields.

We have already referred to the danger of restricting activity to one technique or type of apparatus, which is the inherent danger of the otherwise useful combination of man and machine. It restricts the outlook to that of a worker on a factory conveyor belt. It seems that modern equipment manufacturers are aware of this and try to design multi-informational equipment such as GC/MS apparatus.

Capable analysts have to be aware of everything that is currently going on in analytical chemistry, to improve from time to time their research activity, and

sometimes even to change their field in order to improve their performance. It may be argued that there is already too much for any one person to learn. It is not necessary to be an expert, however; what is needed is a broad general awareness of current events and the ability to assess and relate them critically and intelligently.

Nowadays a gas chromatographer must know about, work, and even research in HPLC. This means enlarging not only his knowledge but the field of investigation as well. However the most important achievement is the comparison and correlation of analytical information. Nature has bestowed upon man, besides the gift of imitation, the gift of comparison. The highest satisfaction for an analyst is obtaining comparable and corroborative information by various experimental methods.

It is for this reason that the "Black-box" of this book has discussed methods that complement or compete with or can replace or be used to check each other. The desire to keep the book short has prevented us from approaching other analytical techniques in the same way; however, we hope we have inoculated the reader with enough curiosity to compare them himself. Comparison of analytical methods allows us to understand them better, and to reach the conclusion that the whole analytical process is one unitary act and that if we want to understand it we have to 'tame' it by perceiving its essential nature.

And now to finish with the first 'C' we discuss a more delicate problem, which is essential for work in the laboratory, especially in the research laboratory. Modern society, except in the more unfortunate parts of the globe, has opened to a great extent the way to education. As with any wide-scale action, this has brought some problems. Were the education system well organized, it should produce only capable specialists. Owing to the need to verify that knowledge has truly been gained, some form of examination is necessary, and because of the human nature of examiners and sometimes because of the limitations of the use of computers in examining methods, the product of the educational process may lie outside the quality tolerances but escape detection in the 'quality-control inspection'. In other words, the universities and colleges sometimes produce graduate chemists and analysts who are less gifted or dedicated and whose ambition is to get a diploma and not to devote themselves to science. Some of them may even pursue graduate studies and get their Ph.D. without improving their capability, and so merely add one more diploma to their collection. This diploma rush is one of the undesirable consequences of the outlook of modern society; individuals whose mercantile spirit prevails over their passion for research are dominated by the desire to occupy a better position in the hierarchy, whether it is justified by ability and performance or not. To be fair, however, it must be added that some students mature more slowly than others, and that students who may appear poor in undergraduate courses sometimes flower remarkably in the forcing-bed of research, whereas some 'bright' students fail to fulfil their early promise and do not come to fruition.

The danger carried by the less capable individuals is latent at first but may grow if, by luck or favourable circumstances, they come to occupy decision-making positions in industry or scientific research. To avoid the mistakes that may ensue in such cases, means must be devised of isolating mediocrity.

One way of doing this is by team-work in research, since the objective of the team is collective effort towards a common goal, and in theory at any rate the free discussion and criticism amongst the members of the team should lead to a mediocre worker feeling 'out of things' and voluntarily leaving the team. The efficiency of team-work in general was discussed in Chapter 2, and here we shall discuss this other aspect of it.

Perhaps no other language has a better equivalent for the English word 'team'. It evokes the idea of a homogeneous group with homogeneous potentials and tendencies. As in sports, one member of the team may substitute for another if occasion demands, the overriding consideration being the performance of the team. The whole will be greater than the parts. It is necessary, however, again as in sports, for the team to be properly managed, trained and coached. The analogy can be carried further, since some teams will be better than others, and for reasons of sentiment, kindheartedness, lack of ruthlessness, or even laziness on the part of the management, some teams may find themselves carrying 'passengers' – the mediocrities that the system was intended to get rid of. Ideally, a member of the team who cannot stand the attitude and rhythm of the rest of the team will leave it, ensuring its health, but the real world is far from ideal, and the mediocre are far more likely to remain than to leave, possibly because their very mediocrity prevents them from perceiving it.

To maintain its vitality, analytical chemistry has to rely, in the first place, on capable people who are in a permanent process of self-improvement.

(b) *Correctness*. This quality is implicitly related to capability through reciprocity. We place it between capability and creativity since it serves as a bridge between them.

This quality is also nurtured in the future specialist while he is still a student. The first facet of this quality is punctuality. As scientists we do not fully agree with the saying 'time is money' but we do consider that punctuality can be educational and can be taught. We all appreciate the English ideals of punctuality and recall with pleasure professors who used to come to and leave classes with the exactness of a clock, so that other classes did not suffer from shortage of time.

We consider that joining and leaving the class at the correct time is a part of the educational process. The professors who give good courses and at the same time are punctual have greater influence than the 'absent-minded' ones who eventually utilize not only the break needed for students to reach another lecture room (or the cloakroom) but several minutes beyond as well.

We suggest that analysts may assume they are correct if they have the vice of punctuality.

This facet of correctness, punctuality, may have unfortunate effects if it is disregarded during international conferences and congresses. Nowadays the extent of these meetings, even if they are organized with very narrow specialization within sessions, requires a mathematical observance of the time prescribed. One of the authors has seen in Japan what 'cosmic' punctuality means during a congress. We consider that participation of youth in this kind of well organized meeting teaches them, among other prerequisites of correctness, what punctuality is.

Many still consider that scientists are strange, absent-minded people, who may be pardoned everything, but such scientists often turn out to be pseudoscientists and their absent-mindedness will affect their research work.

However, correctness does not mean only punctuality. To be correct means to be rigorous in general and in research. Perhaps no other branch of chemistry evidences this better than analytical chemistry, which is a science by the very virtue of its extremely rigorous character. Though punctuality may be learned from others, rigour in research and the skill to obtain 'correct' results are acquired from daily laboratory work.

Statistical calculations show us which of a large number of replicate determinations is most probably closest to the truth. However good the analyst and correct the procedure, random fluctuations in the conditions in the laboratory (equipment performance, reagents, etc.) will cause a variation in the results, and this variation will be a direct measure of the skill of the analyst.

Thus, correctness is no longer only necessary; it is compulsory and must be imposed on the young analyst, the more so if we consider that some day he may have to work with a unique sample, and be unable to perform enough replicate experiments to allow the use of statistics.

Correctness in analytical work is best ensured by frequent analysis of standard reference materials and participation in 'round-robin' collaborative analyses of the same material in various laboratories. Otherwise it is all too easy to fall into the trap of assuming the mantle of infallibility. There are no popes in analysis! Such exercises often reveal unsuspected weaknesses in methods or personal skills [327]. Correctness is the hall-mark of a research team engaged in the forefront of analytical research, and to ensure it, multidisciplinary teams of analysts are more and more often employed, so that the results obtained by different methods can serve to cross-check each other.

To be correct, then, the analyst has to expand his education continually, and work hard to ensure correctness of his results, so that even when part of a team, he can contribute fully to the rigorousness of its research.

Correctness gives people justifiable confidence in themselves and thus increases the likelihood of correctness in their analytical results. The importance of this is obvious if we consider a clinical analysis laboratory supplying inaccurate results through lack of skill or attention to detail on the part of the operators. Such errors could cause irreversible damage.

The conclusion is that to be a good analyst, the scientist must do his best to work correctly and to produce the results on time. Punctuality in supplying the results is especially important in production quality control. It was to minimize the delay in delivery of analytical information and to reduce the enormous amount of skilled labour required for manually performed analyses, that on-line analysis was developed. The role of the analyst has correspondingly shifted from concentration on using manual *and* mental skills to using mental skills only (to ensure correct choice and programming of the instrumentation) and thus having more time for development of ideas.

Automation of analytical processes can help the analyst by ensuring the continuous high-speed acquisition and handling of a large amount of data. No team of analysts, no matter how skilled, could compete with an on-line gas chromatograph or an automatic emission or X-fluorescence spectrum analyser. On the other hand, for a single analysis a competent analyst may often produce a faster and more correct result than the machine can.

Now, since we have built the bridge from the first to the third of the qualities of an analyst, let us consider this third 'C' which is the premier quality of a scientist.

(c) *Creativity*. Of all qualities of a research worker, this is the most important for the development of science. Although throughout this book we have referred to the problem of creativity in science, we take the risk of repeating ourselves and discuss here some general aspects of this quality which is a characteristic of most of the scientific community.

We believe that the scientific creativity of an individual evolves in three stages as follows: undergraduate, graduate and post-doctoral. The present organization of universities in most countries with some educational tradition allows recruitment of students for research teams while they still are undergraduates. This selection requires some care, since the candidates must exhibit, besides solid professional knowledge, remarkable intellectual qualities. In no field of science can the practitioners (as opposed to the researchers) generally create work of real value. A creative scientist must be cultured, must possess a general knowledge established during high-school years. It is general knowledge which develops the imagination, which helps to obtain the right image of nature.

Very often the mistake is made of recruiting researchers from among students according to their examination marks. These are a necessary but not a sufficient criterion. The great scientists of all times have also been great people in themselves. A scientist is an individual with a special mental outlook, quite distinct from that of other intellectual fields. Only those students who throughout the years exhibit distinct thinking ability, and can assimilate information and generalize it correctly and quickly, should be selected for a research career.

A research-oriented student who is to be a future scientist must be quick-witted. This is a quality possessed by a limited number of individuals. To deal with major science, to be creative in it, means to think rapidly and well.

Another essential quality for a scientist is adaptability, within both a certain research subject and a certain research team. We have remarked above that team-work eliminates individuals unsuited for research; thus the most efficient aptitude test for students is assigning them to work with a research team.

The research work of an undergraduate student has in most cases a formative character. The student thus learns how to work in a laboratory. The quality and creativity of this early research leaves a mark upon the future researcher. This brings us again to a subject already discussed throughout this book: the schools of research. These are generally associated with particular departments in universities or research institutes. Although the heads of the research units must themselves be researchers, the enormous volume of paper work very often transforms them into simple 'organizers', which is detrimental to the whole research.

Scientific research of quality is not possible without adequate organization and supervision. However, organization must not be confused with science itself. This confusion would be harmful for science and would in fact disorganize research. To continue the tradition of a research school, the appointed head of that school has to be a passionate and active researcher. The example of the chief influences the whole school of research.

The timing of research, at least for a beginner, is vital. Research cannot be non-stop, for physical and physiological reasons, but it must be continuous. A man of real dedication to science, though permanently preoccupied by science, seeks active, intelligent rest. Thus most researchers have hobbies, e.g. mountaineering and music, whereas practitioners such as physicians may occupy their leisure time with solving difficult problems of mathematics.

For young researchers it is particularly important how they organize their leisure time so as to recover force for research. In this case also, the answer is often given by the team. A good scientific research team is so homogeneous that its members are a team even during leisure time.

A good example is supplied by a famous Romanian school of research, that of the late Professor Nenitescu, known the world over for his research in organic chemistry. Although he imposed on his research team an unceasing 'tough' rhythm (which he observed himself by being always to be found in the laboratory or library), in August he literally forced all the staff, except a laboratory assistant left behind to guarantee the safety of the building, to go on vacation; many of his staff accompanied him on a well-deserved active vacation, most of which was spent hiking and mountaineering. After such a month of rest the work was resumed with renewed vigour.

The student who participates in the various activities of the research team learns not only how to approach problems but how to become a real scientist.

We do not endorse the opinion of some scientists that all the time should be spent in the laboratory and library without any active rest. Life has shown that such scientists are undoubtedly productive for a while, then they get tired, and this may be sensed in their activity.

The research topics to be tackled are very important factors in the development of scientific researchers. We do not agree with the idea that the beginner should deal with unimportant matter, so as not to hamper the research of the team. The young researchers should be involved in the full work of the team right from the start, because quite often they bring new and unbiased outlooks which lead to a better solution or even break a deadlock within the team.

We consider that in the ideal research school the members are so similar in value that any one of them could become the leader and bring the team to its objective, just as any member of an Everest 'summit party' can take the lead successfully.

The second stage of training is the research leading to the Ph.D. As we have already mentioned, these graduate studies are pursued by each student individually (there are no collective Ph.D. degrees and it is unlikely there ever will be); however, these studies may be carried out within a team. A well-constituted team will ensure the high quality of information gathered throughout the graduate studies.

During graduate studies in analytical chemistry, special attention must be paid to giving the student a general culture in analytical chemistry. Although in the United States good graduate work is conducted on ultraspecialized research themes, we consider that, in spite of the fact that graduate studies are a higher stage of education, they are still only a formative stage and that the European tradition of more general doctoral studies should not be abandoned. Thus, during the graduate study years, the future researcher should become acquainted with the various experimental techniques of major importance in analytical chemistry.

We have observed that there are many more Ph.D. dissertations dealing with methods of studying composition than those which approach the problem of structure. It seems to us legitimate to ask why there is this tendency to avoid the problems of structure. The answer may not be too agreeable for most of us; it is simply that these problems are more difficult and many analysts and researchers do not know how to solve them. To approach a problem of structural analysis requires, according to what we have already said in this chapter, analysts of very broad outlook and training, with great insight. In mountaineering parlance, they are the 'tigers' capable of tackling the analytical equivalents of the 'last problems' of climbing the North wall climbs on mountains such as the Eiger in the Swiss Alps.

As might be expected, the analyst who does graduate work on some structural analysis theme may gain great satisfaction when the various experimental fragments are fitted together to provide a complete answer to the problem.

As analysts, unlike physicians or lawyers, cannot put up a brass plate at the door to announce their profession, we may ask what the Ph.D. in analytical chemistry is worth. The answer is that if the Ph.D. was obtained from a good

school it opens the future towards new research, towards scientific thinking in analytical chemistry, towards the third stage.

If this third stage is not of limited duration, research can both profit and be disfavoured by it. In this final stage, only a few will do research which opens new trails and generates new approaches. If we are not among them, we should not feel depressed, and give up, however. In science, things are more difficult than in other fields of human endeavour. A researcher may never discover such a trail, but still do outstanding and important work in major fields, and obtain results that will stand comparison with those of researchers in general. Heyrovský and Walsh both opened up new approaches, but we must not forget that their creations were supported by assiduous development work by many other researchers. The mere accumulation of data can, at a certain point, lead to the development of new techniques - pattern recognition, Fourier transforms and autocorrelation are just a few examples - and this is one of the very few valid examples of Engels's famous dictum in *Anti-Dühring* that a quantitative change can produce a qualitative change (one of the others is the critical mass for atomic fission).

To conclude this section on the qualities of the analyst, without pretending to be fortune-tellers, we make a concession to the human desire to be thought farsighted, and give our opinion on future fields of analytical research.

Although many are faithful to basic research, which must be continuously promoted under the best conditions, we have to realize that analytical chemistry as a science, through its applied side of chemical analysis, is permanently dependent on various industrial branches and technological processes and is therefore required to solve some of their top priority problems. These make severe demands on the quality of both the analyst and the analytical signal.

Examination of the literature shows that the techniques of surface analysis have undergone the most extensive recent development. They were demanded by new materials and new technologies. Although, as we have mentioned, these techniques are still very expensive, as teachers we must do everything to make students aware of them.

The separation techniques will always enjoy further development, and techniques of higher efficiency will very likely be developed in the near future.

Finally, the interaction of analytical chemistry with other fields such as medicine, biology and biochemistry, and research in analytical chemistry itself, will make new demands on the quality of the analytical signal, which will implicitly lead to automation. The automatic techniques will further develop, with favourable effects on human activity.

These problems, as well as automation and its development, are the topic of the next section, which discusses the quality of the analytical signal.

### 3.3.2 Quality of the Analytical Signal – the Three 'R's

The analytical signal can be discussed endlessly, and in this book we have referred

mostly to the output. There has been much theoretical work on the problem of signal and noise, and a good general account of its statistical nature will be found in the recent book by Liteanu and Rîcă [85]. Here we discuss three characteristics of the analytical signal that we consider of major importance: rapidity, reproducibility and reliability, all of which are dependent on the equipment.

(a) *Rapidity.* Throughout the years this concept has undergone several modifications in terms of analytical practice.

When analytical chemistry became an independent science (even though not recognized as such), with the generalization in practice of the classical gravimetric and titrimetric methods, the problem arose of obtaining the result of an analysis as quickly as possible, especially as analytical control became more frequently applied in industrial production. Since at that time there was no automated equipment, the methods themselves had to be adapted. Many of us can recall that before the second world war the most rapid gravimetric methods were often considered to be those which allowed direct weighing of the precipitate after its collection and drying in a filter-crucible. Spacu and co-workers, in the University of Cluj, Romania, introduced in the 1920s the technique of washing the precipitate in the crucible with high-volatility organic solvents, usually alcohol and ether, and drying in vacuum. Even these methods, however, were slow in comparison with some used by analysts in the iron and steel industry, who could determine silicon gravimetrically in 20 minutes (including fuming with sulphuric acid, filtration and ignition!), carbon in 10 minutes and manganese in 7. One of us is still willing to demonstrate to students (against a stopwatch) the determination of copper in brass in 5 minutes or less, from starting to weigh to completion of the titration. However, for modern steel-making plant, with a charge-to-charge turn-round time of only about 40 minutes, even analysis times such as these are far too long, and a complete analysis is required within 2 minutes or even less.

Such modern developments, and the new materials with special properties, such as semiconductors and 'space-age' alloys and ceramics, the development of nuclear techniques and technologies, biological, biomedical and clinical studies, and the recent investigations on extraterrestrial materials, for which the classical techniques are often inapplicable, have required the development of new analytical processes, which by their nature have lent themselves to partial or complete automation, with an attendant increase in the rate of data-acquisition. The strongest catalyst in the development of these laboratory techniques, however, has been the demand for greater analytical control of various branches of production. For efficiency, this requires the adaptation of the techniques to the process, and the automation of the techniques together with feed-back loops for computerized automatic control of the process.

As mentioned earlier, automation in analytical chemistry and in analytical production control has required the mingling of various disciplines, such as physics, electronics, chemistry, mathematics and cybernetics to achieve the 'wonders of the century', the automatic analysers. It has also led to the 'isn't

science wonderful' syndrome, manifested as acceptance of such machinery without close questioning of the validity of the results.

The rapid expansion of industrial production has had some detrimental effects, not always easy to combat. The most emotive of these is pollution of the environment. Although in existence since industry first started, and recognized before the second world war, it was not regarded as a serious problem. Now it is a universal matter of concern, but is often considered purely emotionally, even by scientists. The problem of pollution has resulted in a minor industry in the development of its analytical control, involving the design and application of new methods for continuously monitoring and automatically controlling pollution. This, in turn, has contributed a great deal to the rapid development of automation in analytical chemistry in general.

In Section 3.1, when the sample, sampling, and sample processing were discussed for educational reasons, the discussion was limited to general principles and the importance of 'correct' sampling, with no reference to automatic sampling and to automatic sample-changers. The studies on environmental pollution have made it necessary to devise automatic sampling and analysis systems to ensure adequately precise and rapid analysis. The development of rapid clinical analysis and analytical 'profiles' as aids to diagnosis in medicine has also played a major role in the automation of analysis.

However, the strongest impetus for automation and miniaturization of analytical control has come from the *in situ* studies of the atmosphere and composition of the outer planets, which necessitated completely automatic analysis and relay of the results to Earth. In comparison with this kind of equipment, the problems we have discussed in connection with sampling, sample preparation and analysis may look obsolete. The automatic device takes the sample and analyses it by a variety of methods (mainly non-destructive), processes the data and transmits the report of the results (telemetric analysis).

We mention all this so that the beginner or even a dedicated analyst who has unfortunately not read enough from the literature or is otherwise not up to date, may understand why analyses must be done rapidly and why the notion of a rapid analytical signal is mentioned.

For those who do basic research in various fields of science in general, and chemistry in particular, not only rapid but very rapid analyses are needed, e.g. in studies of reaction kinetics, of isomerism, conformational studies, etc. Dynamic record very fast processes, and sometimes characterize reaction products which are unstable and have very short lifetimes.

Even to the most practised and up-to-date analyst, meeting an automatic analysis device which transmits data continuously can give a shock and raise questions about the future of analytical chemistry. When one of the authors saw, at a street crossing in Kyoto, Japan, an automatic carbon monoxide analyser with digital display of CO concentration in ppm along with a display of the noise

level and temperature, he had brought home to him what a fast analytical signal is, and that the studies of pollution of the environment have pushed analytical chemistry literally onto the street, for the good of mankind.

Let us return to the rapidity of the analytical signal. The need for it we discussed above. However, not every analytical apparatus can give a signal in as short a time as we might desire. For various technical reasons, the analytical signal (the output) will lag behind the sample introduction (the input) by a time interval  $\Delta t$ .

The improvement of equipment for the control of rapid processes aims at ensuring the most rapid signal, i.e. minimizing  $\Delta t$ . Let us take as example one of those we have already used in the book: without the demand for rapid analysis the designing of GC/MS or GC/IR apparatus would have been inconceivable. The analysis of complex mixtures by these techniques may produce several hundred chemical species which have to be separated and analysed and the results produced rapidly. The output signal can no longer be interpreted directly by the analyst himself, since doing so would induce a long delay between signal output and result. Thus, it was necessary to develop a fully automatic device which included adequate electronics to yield the signal rapidly, and a computer to process it fast enough. The GC/MS/computer systems are now an example of automatic, continuous and rapid analysis which represent an ultimate in the development of the analytical process.

To conclude these general considerations of rapidity, let us discuss on-line analysis, which has brought the effectiveness of analytical chemistry to a maximum. On-line analysis of various continuous industrial processes has to be rapid and sometimes very rapid indeed. The rapid signal is hence a prerequisite of automatic on-line process control. Equipment has been produced which is self-calibrating and which, when connected to the on-line computer, becomes a basic factor in optimization of production processes.

Even so, there will always be those who consider that automation continuously lowers the need for analysts. We feel this is the attitude of the uneducated and less competent, driven by self-interest to fear for their own jobs, who ignore what analytical chemistry is, i.e. a science in a continuous state of development. The analyst will always have new problems set by developments in science and technology, and must find new techniques, equipment, and processes to solve them. He will also always seek to improve existing techniques and equipment, to obtain ever higher performance in analytical quality control.

We shall now discuss the other two 'R' characteristics of analytical equipment and the analytical signal, i.e. reproducibility and reliability.

(b) *Reproducibility and Reliability.* We have left these two parameters till last, to conclude this chapter, since reproducibility and reliability are, in our opinion, correlated with respect to analytical chemistry.

Reproducibility of the analytical signal is a prerequisite of good quality equipment. Reliability is a fashionable term, very frequently used by experts in

electronics, and refers to the efficiency of operation of some piece of equipment (the 'safety' in informational jargon).

We cannot speak sensibly about automatic laboratory or on-line equipment if the method involved and the apparatus do not secure reproducibility of the signal. The degree of reproducibility of the signal is related to the method of analysis, the performance of the equipment used, the concentration level of the species concerned, and the nature of the sample. At trace levels the non-destructive methods often give better reproducibility because the problem of contamination is eliminated. The reproducibility of the analytical signal is often regarded as related to the degree of automation of the system used, but this is often a misleading criterion. Many 'old-fashioned' analysts, using manual classical methods can achieve a reproducibility of performance, even for complex samples, that is better than that of even the latest instruments, in certain applications. Of course the reverse also holds, and there are many analyses that are beyond the capability of any manual method, but easy to perform by instrumental methods. However, it is all too easy to say "yes, the errors *are* rather large and the reproducibility poor, but any result is better than no result at all". Instead, there should be a continuous acceptance of the challenge to improve performance and to raise that of instruments and automatic analysers to compare with the best achievements of the 'old-timers'.

Another problem that analysts are not yet accustomed to, but must come to terms with, is reliability. For the manufacturers of high-performance laboratory equipment this is, besides design, the most important problem related to competitiveness of their product. Laboratory equipment has to maintain its level of performance over long periods of time to meet the needs of modern research and analysis. This is especially so for automatic analysis stations, e.g. 'background pollution' stations placed at high altitude to sample aerosol pollutants of the environment. These stations generally need to work non-stop for about a month (i.e. give constant analytical conditions) from start to stop, and that the results are comparable.

The problem of reliability is most stringent in automatic equipment (XRF, GC/MS) for outer space analyses. The reliability of this equipment has to be practically absolute in order to ensure continuous function and the relay of data to the mission control centre.

These considerations bring to an end our short discussion on the analytical signal. Here, as in the sections dealing with the qualities of the analyst, we have restricted the discussion to certain aspects. These three criteria of signal quality are wholly interdependent. To obtain a rapid and reproducible signal, only highly reliable equipment must be used. Likewise, the rapidity of the signal can be continuously improved by improvement of the electronics and the mechanical system, checked by testing the reliability of each component.

The reproducibility of results has always been a main concern (and a means

of self-examination and a source of pride) for analysts, but they should never really be satisfied by the performance of the equipment available, and should always seek to do still better.

These qualities of the analytical signal will cause some methods or makes of equipment to be preferred to others, without eliminating them. It is up to the analyst to select the most adequate method, the most suitable for reaching the final goal. It is this ability that differentiates between analysts just as performance does laboratory equipment. It is the function of teaching and education to bring the analyst to see this, and so to ensure that we continue to progress.

# Afterword

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## *A look into the future*

When the writing of a book is finished and the outcome inspected, the author(s) will always have the feeling that at least some chapters or sections would come out better if they were to be written again. This is the more so when the topic of the book refers to education, in whatever field. Since as far as we are aware this is the first book of its kind in analytical chemistry, we have tried to be original in its conception. However, we realize that we have succeeded only partially in discussing education in and through analytical chemistry. We hope that, at least in part, we succeed in enticing the freshman in chemistry to this endless discipline which is analytical chemistry, and to convince the dedicated analyst that his choice is the best and that it pays to persevere in improving the results.

Now, in very few books on any field of scientific research, will you find forecasts of future development of that field. Although there are at present a lot of futurologists, we personally do not know anyone who can tell the fortune of analytical chemistry. However, we will try, based on the knowledge we have accumulated, to look into the future of this discipline, or rather to present some of its highlights that have the most likely prospect of development.

Basic analytical chemistry research will certainly keep many people busy. New reactions and new reagents will always be studied; this will ensure, besides a reserve of sensitive and selective reactions, the enrichment of the traditional 'bank' of analytical chemistry. New kinetic and enzymatic reactions, bioluminescent and chemiluminescent reactions will be discovered. The future experts in analytical chemistry will need to devise new physical methods of analysis which will complement or supplant the old ones. Given the present role of analytical chemistry in the control of very diverse technological processes, these new methods will have to be compatible with the operational parameters of the processes. The control apparatus will be operated by microprocessor and computer, and will be an integral part of the production process, capable of self-control and self-repair.

Since at least some of this equipment will be available in the near future,

analysts will soon have more time to think, and the more they think, the more substantially will they contribute to promotion of their field.

The increasing automation of equipment will force all analysts to develop new methods of analysis and to expand the theoretical foundations of analytical chemistry.

In order to develop analytical chemistry, all countries, at least in their large educational establishments, will have to develop independent departments of analytical chemistry. Wherever absent, research institutes of analytical chemistry will have to be created.

Although there are multilingual journals of analytical chemistry, we think they are too few. Further, we feel strongly that the important papers should be published only in languages generally used internationally; otherwise their value is severely limited by the language barrier. Attempts to eliminate the traditional method of publication will fail, because this is the only way which can give a reasonable certainty that the material published is in fact correct (provided the editors do their job properly), but refereeing must become much more critical, to keep useless information out of the literature, and mitigate the problem of information retrieval. It is also the case that facts buried in the body of the paper (but excluded from the abstracts) may be of great use to others. Many workers believe in looking at the papers immediately before and after the one of interest, in the hope of a lucky 'find'.

The exchange of information regarding analytical chemistry will have to be amplified. We think such exchange is most efficiently done by direct contact between analysts, especially the younger ones, by participation in international meetings, and this should be encouraged. The Euroanalysis meetings should be organized on a triennial basis. As the name implies, the attendance at the Euroanalysis meetings is indeed practically only European, which is unfortunate, as greater overseas participation would be of great value. The chemistry societies and other national and international bodies will have to direct their efforts towards making such meetings truly international; we are sure funds for this purpose will be found. Exchange of specialists between various countries will also have to be intensified and the number of doctoral and postdoctoral scholarships increased.

These requirements will be fulfilled only when analysts the whole world over unite and fight with dedication for the promotion of teaching, research and education in analytical chemistry.

Nothing is now left but to say, as Caesar did when he crossed the Rubicon, "*Alea jacta est!*". We are sure there will be many criticisms of the opinions and ideas advanced in this book; indeed we hope so, because it is only by free discussion and debate that real progress can be made. We therefore express in advance our gratitude to all those stimulated to further the cause of analytical chemistry, and especially those who will help us by letting us know their own

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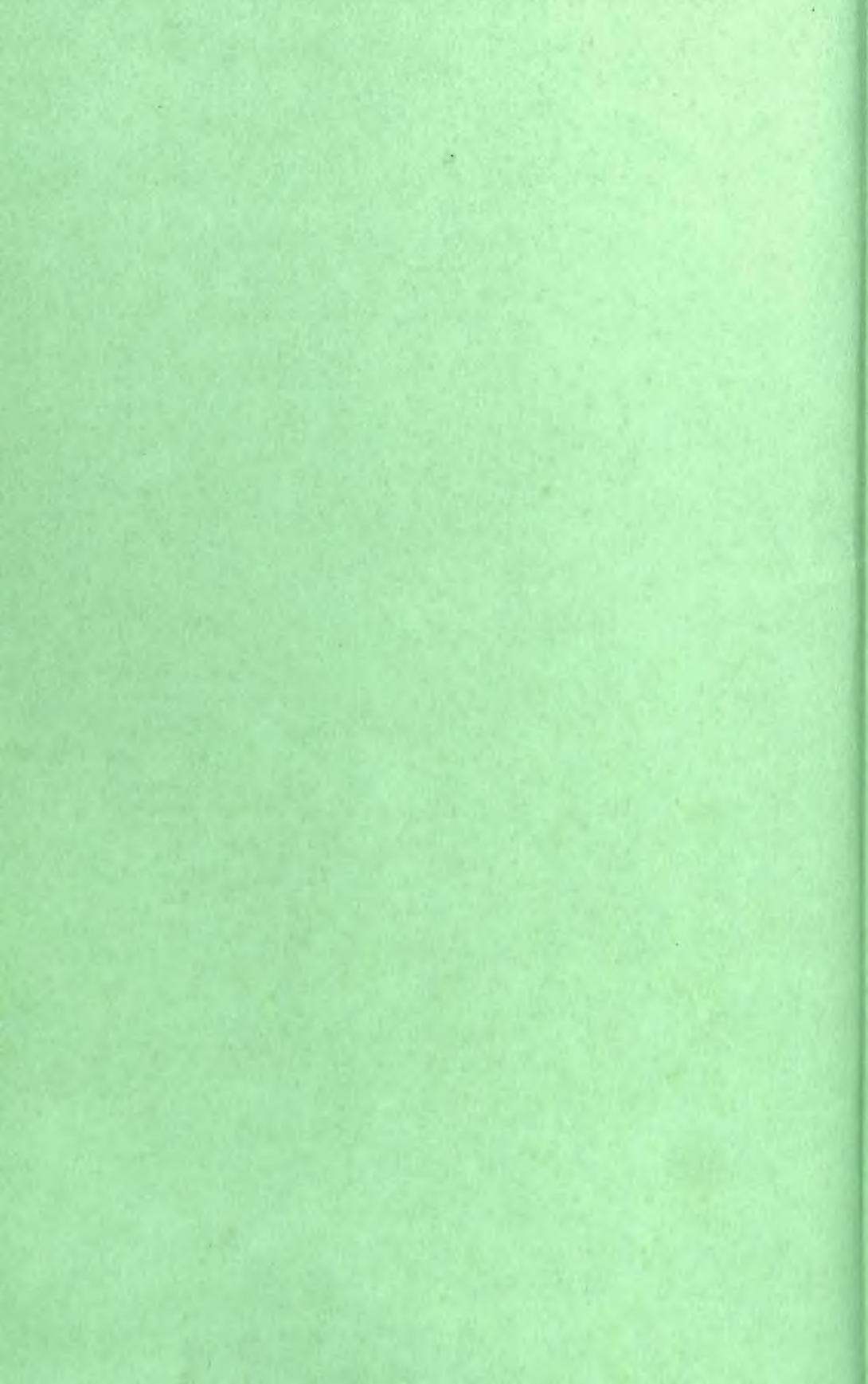
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